



HFW

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 02-249-E (400.042))

In the Application of:

Beigelman et al.

Serial No.: 10/669,841

Filing Date: September 23, 2003

For: Oligonucleotide Mediated Inhibition of
Hepatitis B Virus and Hepatitis C Virus
Replication

Examiner: TBD

Group Art Unit: 1632

Confirmation No.: 2643

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

TRANSMITTAL LETTER

In regard to the above identified application:

1. We are transmitting herewith the attached papers for the above identified new patent application:

- ☒ Information Disclosure Statement;
- ☒ Information Disclosure Statement (IDS) PTO-1449 Form;
- ☒ Copies of IDS Citations for S/N 10/669,841 (Total 54 foreign patents and 323 other documents); and
- ☒ Return Receipt Postcard.

2. With respect to additional fees, no additional fee is required.

3. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.

4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1 hereinabove, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450 on August 3, 2004.

By :

Anita J. Terpstra
Reg. No. 47,132

McDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 SOUTH WACKER DRIVE
CHICAGO, ILLINOIS 60606
TELEPHONE (312) 913-0001
FACSIMILE: (312) 913-0002



PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 02-249-E (400.042))**

In the Application of:)	
)	
Beigelman et al.)	
)	Examiner: TBD
Serial No.: 10/669,841)	
)	Group Art Unit: 1632
Filing Date: September 23, 2003)	
)	Confirmation No.: 2643
For: Oligonucleotide Mediated Inhibition of)	
Hepatitis B Virus and Hepatitis C Virus)	
Replication)	

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the cited references are enclosed. These references are also listed on the enclosed PTO Form 1449.

Also, attached to each reference in a language other than English is a translation of the reference in accordance with 37 C.F.R. § 1.98 (a) (3)(ii).

As this Information Disclosure Statement is being submitted after receipt of a foreign search report, a copy of the search report is attached herewith.

In the judgment of the undersigned, portions of the listed references may be material to the Examiner's consideration of the presently pending claims. This statement is not a

representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

Applicants do not believe any fee is due with this submission. If this belief is in error and the Patent Office determines that the fee prescribed in the relevant portion of 37 C.F.R. Section 1.97 is applicable, the undersigned attorney by his signature hereby authorizes any such fee to be debited from Deposit Account 13-2490.

U. S. PATENT DOCUMENTS

- * Draper et al., U.S. Patent Application No. 07/882,712, filed May 14, 1992
- * Draper et al., U.S. Patent Application No. 08/193,627, filed February 7, 1994
- * Ludwig et al., U.S. Patent Application No. 08/878,640, filed June 19, 1997
- * Sullenger et al., U.S. Patent Application No. 09/205,520, filed December 3, 1998
- * Blatt et al., U.S. Patent Application No. 09/257,553, filed February 24, 1999
- * Blatt et al., U.S. Patent Application No. 09/274,553, filed March 23, 1999
- * Draper et al., U.S. Patent Application No. 09/436,430, filed November 9, 1999
- * Beigelman et al., U.S. Patent Application No. 09/476,387, filed December 30, 1999
- * Blatt et al., U.S. Patent Application No. 09/504,321, filed February 15, 2000
- * Draper et al., U.S. Patent Application No. 09/531,025, filed March 20, 2000
- * Blatt et al., U.S. Patent Application No. 09/611,931, filed July 7, 2000
- * Draper et al., U.S. Patent Application No. 09/636,385, filed August 9, 2000
- * Draper et al., U.S. Patent Application No. 09/696,347, filed October 24, 2000
- * Blatt et al., U.S. Patent Application No. 09/740,332, filed December 18, 2000
- * Blatt et al., U.S. Patent Application No. 09/817,879, filed March 26, 2001
- * Draper et al., U.S. Patent Application No. 09/877,478, filed June 8, 2001
- * Usman et al., U.S. Patent Application No. 09/877,526, filed June 8, 2001
- * Beigelman et al., U.S. Patent Application No. 09/918,728, filed July 31, 2001
- * Thompson et al., U.S. Patent Application No. 60/082,404, filed April 20, 1998
- * McSwiggen et al., U.S. Patent Application No. 60/083,217, filed April 27, 1998
- * Blatt et al., U.S. Patent Application No. 60/100,842, filed September 18, 1998
- * Hartmann et al., U.S. Patent Application No. 60/101,174, filed September 21, 1998

- * Macejak et al., U.S. Patent Application No. 60/296,876, filed June 8, 2001
- * Morrissey et al., U.S. Patent Application No. 60/337,055, filed December 5, 2001
- * Macejak et al., U.S. Patent Application No. 60/355,059, filed December 24, 2001
- * Beigelman et al., U.S. Patent Application No. 60/358,580, filed February 20, 2002
- * Beigelman et al., U.S. Patent Application No. 60/363,124, filed March 11, 2002

U.S. PATENT DOCUMENTS

- * Suhadolnik et al., U.S. Patent No. 4,859,768, issued August 22, 1989
- * Suhadolnik et al., U.S. Patent No. 4,924,624, issued May 15, 1990
- * Cech et al., U.S. Patent No. 4,987,071, issued January 22, 1991
- * Suhadolnik et al., U.S. Patent No. 5,188,897, issued February 23, 1993
- * Sproat, U.S. Patent No. 5,334,711, issued August 22, 1994
- * Suhadolnik et al., U.S. Patent No. 5,405,939, issued April 11, 1995
- * Gold et al., U.S. Patent No. 5,475,096, issued December 12, 1995
- * McSwiggen et al., U.S. Patent No. 5,525,468, issued June 11, 1996
- * Suhadolnik et al., U.S. Patent No. 5,550,111, issued August 27, 1996
- * Suhadolnik et al., U.S. Patent No. 5,556,840, issued September 17, 1996
- * Gold et al., U.S. Patent No. 5,567,588, issued October 22, 1996
- * Torrence et al., U.S. Patent No. 5,583,032, issued December 10, 1996
- * Shih et al., U.S. Patent No. 5,589,332, issued December 3, 1996
- * Draper et al., U.S. Patent No. 5,610,054, issued March 11, 1997
- * Noonberg et al., U.S. Patent No. 5,624,803, issued April 29, 1997
- * Been et al., U.S. Patent No. 5,625,047, issued April 29, 1997
- * Usman et al., U.S. Patent No. 5,627,053, issued May 6, 1997
- * Chowira & McSwiggen, U.S. Patent No. 5,631,359, issued May 20, 1997
- * Long et al., U.S. Patent No. 5,633,133, issued May 27, 1997
- * Suhadolnik et al., U.S. Patent No. 5,643,889, issued July 1, 1997
- * Cook et al., U.S. Patent No. 5,670,633, issued September 23, 1997
- * Eckstein et al., U.S. Patent No. 5,672,695, issued September 30, 1997
- * Suhadolnik et al., U.S. Patent No. 5,700,785, issued December 23, 1997
- * Beigelman et al., U.S. Patent No. 5,716,824, issued February 10, 1998

- * George et al., U.S. Patent No. 5,741,679, issued April 21, 1998
- * Buhr et al., U.S. Patent No. 5,792,847, issued August 11, 1998
- * Joyce et al., U.S. Patent No. 5,807,718, issued September 15, 1998
- * Stinchcomb et al., U.S. Patent No. 5,817,796, issued October 6, 1998
- * George et al., U.S. Patent No. 5,834,186, issued November 10, 1998
- * Arrow et al., U.S. Patent No. 5,849,902, issued December 15, 1998
- * Sullenger and Cech, U.S. Patent No. 5,854,038, issued December 29, 1998
- * Hunt et al., U.S. Patent No. 5,859,226, issued January 12, 1999
- * Suhadolnik et al., U.S. Patent No. 5,863,505, issued January 26, 1999
- * Draper et al., U.S. Patent No. 5,869,253, issued February 9, 1999
- * Nathan et al., U.S. Patent No. 5,871,914, issued February 16, 1999
- * Crooke, U.S. Patent No. 5,898,031, issued April 27, 1999
- * Budowsky et al., U.S. Patent No. 5,962,431, issued October 5, 1999
- * Arrow et al., U.S. Patent No. 5,989,912, issued November 23, 1999
- * Brennan, U.S. Patent No. 6,001,311, issued December 14, 1999
- * Cook et al., U.S. Patent No. 6,005,087, issued December 21, 1999
- * Draper et al., U.S. Patent No. 6,017,756, issued January 25, 2000
- * Crooke, U.S. Patent No. 6,107,094, issued August 22, 2000
- * Eckstein et al., U.S. Patent No. 6,127,173, issued December 3, 2000
- * Usman et al., U.S. Patent No. 6,159,714, issued December 12, 2000
- * Gold et al., U.S. Patent No. 6,300,074, issued October 9, 2001
- * Buhr et al., U.S. Patent No. 6,476,205, issued November 5, 2002

FOREIGN PATENT DOCUMENTS

1. Hampel et al., European Patent No. EP 0 360 257, published March 28, 1990
2. Yamada et al., Japanese Patent No. JP 07231784, published
3. Beigelman et al., International Publication No. PCT/US02/09187, published March 26, 2002
4. Rossi et al., International Publication No. WO 91/03162, published March 21, 1991
5. Eckstein et al., International Publication No. WO 92/07065, published April 30, 1992
6. Usman et al., International Publication No. WO 93/15187, published August 5, 1993
7. Sullivan et al., International Publication No. WO 93/23057, published November 25, 1993

8. Draper et al., International Publication No. WO 93/23569, published November 25, 1993
9. Sullivan et al., International Publication No. WO 94/02595, published February 3, 1994
10. Draper et al., International Publication No. WO 95/04818, published February 16, 1995
11. Usman et al., International Publication No. WO 95/11304, published April 27, 1995
12. Draper et al., International Publication No. WO 95/13380, published April 27, 1995
13. Goldenberg et al., International Publication No. WO 95/22600, published August 24, 1995
14. Stinchcomb et al., International Publication No. WO 95/23225, published August 31, 1995
15. Ansell et al., International Publication No. WO 96/10390, published April 11, 1996
16. Choi et al., International Publication No. WO 96/10391, published April 11, 1996
17. Holland et al., International Publication No. WO 96/10392, published April 11, 1996
18. Kay et al., International Publication No. WO 96/18419, published June 20, 1996
19. Beigelman et al., International Publication No. WO 96/18736, published June 20, 1996
20. Collins et al., International Publication No. WO 96/19577, published June 27, 1996
21. Pyle et al., International Publication No. WO 96/22689, published August 1, 1996
22. Goldenberg et al., International Publication No. WO 97/08309, published March 6, 1997
23. Wincott et al., International Publication No. WO 97/26270, published July 24, 1997
24. Barber et al., International Publication No. WO 97/32018, published September 4, 1997
25. Woolf et al., International Publication No. WO 98/13526, published April 2, 1998
26. Breaker et al., International Publication No. WO 98/27104, published June 25, 1998
27. Karpeisky et al., International Publication No. WO 98/28317, published July 2, 1998
28. Breaker et al., International Publication No. WO 98/43993, published October 8, 1998
29. Ludwig et al., International Publication No. WO 98/58058, published December 23, 1998
30. Deschamps de Paillette, International Publication No. WO 99/07409, published February 18, 1999
31. Wengel et al., International Publication No. WO 99/14266, published March 25, 1999
32. Vierling, International Publication No. WO 99/16307, published April 8, 1999
33. Eckstein et al., International Publication No. WO 99/16871, published April 8, 1999
34. Lu, International Publication No. WO 99/20641, published April 29, 1999
35. Sullenger et al., International Publication No. WO 99/29842, published June 17, 1999
36. Barry et al., International Publication No. WO 99/31262, published June 24, 1999
37. Fire et al., International Publication No. WO 99/32619, published July 1, 1999

374. Graham et al., International Publication No. WO 99/49029, published September 30, 1999
375. Waterhouse et al., International Publication No. WO 99/53050, published October 21, 1999
38. Thompson et al., International Publication No. WO 99/54459, published October 28, 1999
39. Beigelman et al., International Publication No. WO 99/55857, published November 4, 1999
376. Heifetz et al., International Publication No. WO 99/61631, published December 2, 1999
40. Plaetinck et al., International Publication No. WO 00/01846, published January 13, 2000
41. Kao et al., International Publication No. WO 00/04141, published January 27, 2000
42. Torrence et al., International Publication No. WO 00/14219, published March 16, 2000
43. Nathan and Ellington, International Publication No. WO 00/24931, published May 4, 2000
44. Breaker et al., International Publication No. WO 00/26226, published May 11, 2000
45. Kreutzer et al., International Publication No. WO 00/44895, published August 3, 2000
46. Li et al., International Publication No. WO 00/44914, published August 3, 2000
47. O'Hare and Normand, International Publication No. WO 00/53722, published September 14, 2000
377. Pachuk et al., International Publication No. WO 00/63364, published October 26, 2000
48. Wengel et al., International Publication No. WO 00/66604, published November 9, 2000
49. Mello and Fire, International Publication No. WO 01/29058, published October 13, 2001
50. Zernicka-Goetz et al., International Publication No. WO 01/36646, published May 25, 2001

OTHER DOCUMENTS

51. Abramovitz et al., "Catalytic Role of 2'-Hydroxyl Groups Within a Group II Intron Active Site," Science 271:1410-1413 (1996)
52. Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," Trends Cell Biol. 2:139-144 (1992)
53. Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a *retro-inverso* delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons," Nucleic Acids Research 26:4910-4916 (1998)
54. Alter, "Chronic Consequences of Non-A, Non-B Hepatitis," *Current Perspectives in Hepatology*, pp. 83-89 (1989)

55. Baenziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," *Cell* 22:611-620 (1980)
56. Banerjee and Turner, "The Time Dependence of Chemical Modification Reveals Slow Steps in the Folding of a Group I Ribozyme," *Biochemistry* 34:6504-6512 (1995)
57. Bartel and Szostak, "Isolation of New Ribozymes from a Large Pool of Random Sequences," *Science* 261:1411-1418 (1993)
58. Bass, "The short answer," *Nature* 411:428-429 (2001)
59. Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," *Tetrahedron* 49:1925-1963 (1993)
60. Beaudry and Joyce, "Directed Evolution of an RNA Enzyme," *Science* 257:635-641 (1992)
61. Beck and Nassal, "Efficient hammerhead ribozyme-mediated cleavage of the structured hepatitis B virus encapsidation signal *in vitro* and in cell extracts, but not in intact cells," *Nucleic Acids Res.*, 23(24), 4954-62 (1995)
62. Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," *The Journal of Biological Chemistry* 270:25702-25708 (1995)
63. Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-Ribozymes," *Nucleosides & Nucleotides* 16:951-954 (1997)
64. Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," *Bioconjugate Chem.* 8:204-212 (1997)
65. Bernstein et al., "Role for a Bidentate Ribonuclease in the Initiation Step of RNA Interference," *Nature* 409:363-366 (2001)
66. Berzal-Herranz et al., "Essential nucleotide sequences and secondary structure elements of the hairpin ribozyme," *EMBO J.* 12:2567-2574 (1993)
67. Berzal-Herranz et al., "In vitro selection of active hairpin ribozymes by sequential RNA-catalyzed cleavage and ligation reactions," *Genes & Development* 6:129-134 (1992)
68. Bevilacqua et al., "A Mechanistic Framework for the Second Step of Splicing Catalyzed by the *Tetrahymena* Ribozyme," *Biochemistry* 35:648-568 (1996)

69. Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," *Journal of Pharmaceutical Sciences* 87:1308-1315 (1998)
70. Boado, "Antisense drug delivery through the blood-brain barrier," *Advanced Drug Delivery Reviews* 15:73-107 (1995)
71. Bock et al., "The Enhancer I Core Region Contributes to the Replication Level of Hepatitis B Virus In Vivo and In Vitro," *Jour. of Virology* 74:2193-2202 (2000)
72. Borden, "Interferons—Expanding Therapeutic Roles," *The New England Journal of Medicine* 326(22):1491-1493 (1992)
73. Breaker and Joyce, "Inventing and improving ribozyme function: rational design versus iterative selection methods," *TIBTECH* 12:268-275 (1994)
74. Breaker et al., "A DNA enzyme with Mg^{2+} -dependent RNA phosphoesterase activity," *Chemistry & Biology* 2(10):655-660 (1995)
75. Breaker, "Are engineered proteins getting competition from RNA?" *Current Opinion in Biotechnology* 7:442-448 (1996)
76. Breaker, "Catalytic DNA: in training and seeking employment," *Nature Biotechnology* 17:422-423 (1999)
77. Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," *Biotechnology and Bioengineering (Combinatorial Chemistry)* 61:33-45 (1998)
78. Brody and Gold, "Aptamers as therapeutic and diagnostic agents," *Reviews in Molecular Biotechnology* 74:5-13 (2000)
79. Brown et al., "Secondary structure of the 5' nontranslated regions of hepatitis C virus and pestivirus genomic RNAs," *Nucleic Acids Research* 20:5041-5045 (1992)
80. Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," *Biochemistry* 35:14090-14097 (1996) (volume no. mistakenly listed as 6)
81. Burke et al., "Structural Analysis and Modifications of the Hairpin Ribozyme," *Nucleic Acids and Molecular Biology*, edited by Eckstein and Lilley, Springer-Verlag Berlin Heidelberg, 10:129-143 (1996)
82. Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," *Bioorganic & Medicinal Chemistry* 5:1999-2010 (1997)

83. Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," Methods in Enzymology 211:3-19 (1992)
84. Cech et al., "Representation of the secondary and tertiary structure of group I introns," Nature Structural Biology 1:273-280 (1994)
85. Cech, "Ribozymes and Their Medical Implications," JAMA 260:3030-3034 (1988)
86. Chartrand et al., "An oligodeoxyribonucleotide that supports catalytic activity in the hammerhead ribozyme domain," Nucleic Acids Research 23(20):4092-4096 (1995)
87. Charubala and Pfeleiderer, "Chemical Synthesis of 2',5'-Oligoadenylate Analogues," Progress in Molecular and Subcellular Biology 14:114-138 (1994)
88. Chebath & Revel, "The 2-5 A System: 2-5 A Synthetases, Isospecies and Functions," *Interferon: Principles and Medical Applications* pp225-236 (1992)
89. Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Conserved HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Against Most Presently Sequenced HIV-1 Isolates," Nucleic Acids Research 20:4581-4589 (1992)
90. Chen et al., "Probing Immune Functions in RAG-deficient Mice," Current Biology 6:313-319 (1994)
91. Choo et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome," Science 244:359-362 (1989)
92. Chowrira et al., "*In Vitro* and *in Vivo* Comparison of Hammerhead, Hairpin, and Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," J. Biol. Chem. 269:25856-25864 (1994)
93. Chowrira et al., "Novel guanosine requirement for catalysis by the hairpin ribozyme," Nature 354:320-322 (1991)
94. Christoffersen and Marr, "Ribozymes as Human Therapeutic Agents," J. Med. Chem. 38:2023-2037 (1995) (also referred to as Christofferson and Marr)
95. Christoffersen et al., "Application of computational technologies to ribozyme biotechnology products," Journal of Molecular Structure (Theochem) 311:273-284 (1994) (maybe referred to as Christofferson)
96. Colacino and Staschke, "The Identification and Development of Antiviral Agents....," Progress in Drug Research 50:259-322 (1998)

97. Collins and Olive, "Reaction Conditions and Kinetics of Self-Cleavage of a Ribozyme Derived From *Neurospora* VS RNA," Biochemistry 32:2795-2799 (1993)
98. Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," The Journ. of Biol. Chem. 257:939-945 (1982)
99. Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal *versus* Subcutaneous Administration," Clinical Cancer Research 5:2330-2337 (1999)
100. Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit gene function," Trends In Genetics 12:510-515 (1996)
101. Cribier et al., "*In vitro* infection of peripheral blood mononuclear cells by hepatitis C virus," Journal of General Virology 76:2485-2491 (1995)
102. Crooke, "Advances in Understanding the Pharmacological Properties of Antisense Oligonucleotides," Advances in Pharmacology 40:1-49 (1997)
103. Crooke, "Antisense Therapeutics," Biotechnology and Genetic Engineering Reviews 15:121-157 (1998)
104. Crooke, "Progress in Antisense Technology: The End of the Beginning," Methods in Enzymology 313:3-45 (1999)
105. D'Amico et al., "Survival and Prognostic Indicators in Compensated and Decompensated Cirrhosis," Digestive Diseases and Sciences 31(5):468-475 (1986)
106. Daniels et al., "Two Competing Pathways for Self-splicing by Group II Introns: A Quantitative Analysis of *in Vitro* Reaction Rates and Products," J. Mol. Biol. 256:31-49 (1996)
107. Dash et al., "Transfection of HepG2 Cells with Infectious Hepatitis C Virus Genome," American Journal of Pathology 151(2):363-373 (1997)
108. Davis and Lim, "Current Status of Interferon Therapy for Chronic Hepatitis C: A Hepatologist's Perspective," Infectious Agents and Disease 2:150-154 (1993)
109. Davis et al., "Treatment of Chronic Hepatitis C with Recombinant Interferon Alfa," The New England Journal of Medicine 321(22):1501-1506 (1989)
110. Delihais et al., "Natural antisense RNA/target RNA interactions: Possible models for antisense oligonucleotide drug design," Nature Biotechnology 15:751-753 (1997)

111. Diaz et al., "Structure of the Human Type-I Interferon Gene Cluster Determined from a YAC Clone Contig," Genomics 22:540-552 (1994)
112. Doherty and Doudna, "Ribozyme Structures and Mechanisms," Annu. Rev. Biophys. Biomol. Struct. 30:457-475 (2001)
113. Dreyfus, "Restriction Ribozymes?" Einstein Quarterly Journal of Biology and Medicine 6:92-93 (1988)
114. Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular Suppression of Human Immunodeficiency Virus Type I Expression," Journal of Virology 66:1432-1441 (1992)
115. Dusheiko et al., "Sequence variability of hepatitis C virus and its clinical relevance," Journal of Viral Hepatitis 1:3-15 (1994)
116. Duval-Valentin, "Specific inhibition of transcription by triple helix-forming oligonucleotides," Proc. Natl. Acad. Sci. USA 89:504-508 (1992)
117. Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," Biopolymers 48:39-55 (1998)
118. Egholm et al., "PNA hybridizes to complementary oligonucleotides obeying the Watson-Crick hydrogen-bonding rules," Nature 365:566-568 (1993)
119. Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," Nature 411:494-498 (2001)
120. Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in *Drosophila Melanogaster* Embryo Lysate," The EMBO Journal 20:6877-6888 (2001)
121. Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," Genes and Development 15:188-200 (2001)
122. Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in Delivery Strategies for Antisense Oligonucleotide Therapeutics, edited by Akhtar, CRC Press, pp. 17-220 (1995)
123. Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," Proc. Natl. Acad. Sci. USA 87:6743-6747 (1990)
124. Emerich et al., "Biocompatibility of Poly (DL-Lactide-co-Glycolide) Microspheres Implanted Into the Brain," Cell Transplantation 8:47-58 (1999)

125. Farci et al., "A Long-Term Study of Hepatitis C Virus Replication in Non-A, Non-B Hepatitis," The New England Journal of Medicine 325(2):98-104 (1991)
126. Feldstein et al., "Two sequences participating in the autolytic processing of satellite tobacco ringspot virus complementary RNA," Gene 82:53-61 (1989)
127. Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in *Caenorhabditis Elegans*," Nature 391:806-811(1998)
128. Fire, "RNA-triggered Gene Silencing," TIG 15:358-363(1999)
129. Fish et al., "The Role of Three Domains in the Biological Activity of Human Interferon- α ," Journal of Interferon Research 9:97-114 (1989)
130. Forster and Altman, "External Guide Sequences for an RNA Enzyme," Science 249:783-786 (1990)
131. Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," Proc. Natl. Acad. Sci. USA 83:9373-9377 (1986) [sometimes referred to as Frier]
132. Galun et al., "Hepatitis C Virus Viremia in SCID \rightarrow BNX Mouse Chimera," The Journal of Infectious Diseases 172:25-30 (1995)
133. Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," Nucleic Acids Research 21:2867-2872 (1993)
134. Genbank Accession No. AF100308.1
135. Genbank Accession No. D11168
136. Genbank Accession No. D50483.1
137. Genbank Accession No. L38318
138. Genbank Accession No. S82227
139. Gold et al., "Diversity of Oligonucleotide Functions," Annu. Rev. Biochem. 64:763-797 (1995)
140. Good et al., "Expression of small, therapeutic RNAs in human nuclei," Gene Therapy 4:45-54 (1997)

141. Grasby et al., "Purine Functional Groups in Essential Residues of the Hairpin Ribozyme Required for Catalytic Cleavage of RNA," Biochemistry 34:4068-4076 (1995)
142. Griffin et al., "Group II intron ribozymes that cleave DNA and RNA linkages with similar efficiency, and lack contacts with substrate 2'-hydroxyl groups," Chemistry & Biology 2:761-770 (1995)
143. Griffin et al., "Group II intron ribozymes that cleave DNA and RNA linkages with similar efficiency, and lack contacts with substrate 2'-hydroxyl groups," Chemistry & Biology 2:761-770 (1995)
144. Guerrier-Takada et al., "The RNA Moiety of Ribonuclease P Is the Catalytic Subunit of the Enzyme," Cell 35:849-857 (1983)
145. Guidos et al., "Development of CD4⁺ CD8⁺ Thymocytes in RAG-deficient Mice Through a T Cell Receptor β Chain-independent Pathway," J. Exp. Med. 181:1187-1195 (1995) [mistakenly referred to as Guidas]
146. Guidotti et al., "High-Level Hepatitis B Virus Replication in Transgenic Mice," Journal of Virology 69:6158-6169 (1995)
147. Guo and Collins, "Efficient *trans*-cleavage of a stem-loop RNA substrate by a ribozyme derived from *Neurospora* VS RNA," EMBO J. 14:368-376 (1995)
148. Hall, "Monoclonal Antibodies at Age 20: Promise at Last?," Science 270:915-916 (1995)
149. Hammann et al., "Length Variation of Helix III in a Hammerhead Ribozyme and Its Influence on Cleavage Activity," Antisense & Nucleic Acid Drug Development 9:25-31 (1999)
150. Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in *Drosophila* Cells," Nature 404:293-296 (2000)
151. Hampel and Tritz, "RNA Catalytic Properties of the Minimum (-)sTRSV Sequence," Biochemistry 28:4929-4933 (1989)
152. Hampel et al., "'Hairpin' Catalytic RNA Model: Evidence for Helices and Sequence Requirement for Substrate RNA," Nucleic Acids Research 18:299-304 (1990)
153. Harada et al., "Characterization of an established human hepatoma cell line constitutively expressing non-structural proteins of hepatitis C virus by transfection of viral cDNA," Journal of General Virology 76:1215-1221 (1995)

154. Harris et al., "Identification of phosphates involved in catalysis by the ribozyme RNase P RNA," RNA 1:210-218 (1995)
155. Haseloff and Gerlach, "Sequences required for self-catalysed cleavage of the satellite RNA of tobacco ringspot virus," Gene 82:43-52 (1989)
156. Haseloff and Gerlach, "Simple RNA Enzymes with New and Highly Specific Endoribonuclease Activities," Nature 334:585-591 (1988)
157. Hayashi et al., "*In Vivo* Transfection of Rat Liver with Hepatitis C Virus cDNA Using Cationic Liposome-Mediated Gene Delivery," *HCD Gene Delivery* pp143-149 (1995)
158. Hegg et al., "Kinetics and Thermodynamics of Intermolecular Catalysis by Hairpin Ribozymes," Biochemistry 34:15813-15828 (1995)
159. Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," *Science* 287:820-825 (2000)
160. Herschlag and Cech, "Catalysis of RNA Cleavage by the *Tetrahymena thermophila* Ribozyme 1. Kinetic Description of the Reaction of an RNA Substrate Complementary to the Active Site," Biochemistry 29:10159-10171 (1990)
161. Herschlag and Cech, "Catalysis of RNA Cleavage by the *Tetrahymena thermophila* Ribozyme. 2. Kinetic Description of the Reaction of an RNA Substrate That Forms a Mismatch at the Active Site," Biochemistry 29:10172-10180 (1990)
162. Hertel et al., "A Kinetic Thermodynamic Framework for the Hammerhead Ribozyme Reaction," Biochemistry 33:3374-3385 (1994)
163. Hertel et al., "Numbering System for the Hammerhead," Nucleic Acids Research 20:3252 (1992)
164. Hiramatsu et al., "HCV cDNA transfection to HepG2 cells," Journal of Viral Hepatitis 4:61-67 (1997) [sometimes referred to as Hiramatsu]
165. Hofland and Huang, "Formulation and Delivery of Nucleic Acids," *Handbook of Exp. Pharmacol.* 137:165-192 (1999)
166. Honda et al., "A Phylogenetically Conserved Stem-Loop Structure at the 5' Border of the Internal Ribosome Entry Site of Hepatitis C Virus is Required for Cap-Independent Viral Translation," *Journal of Virology* 73:1165-1174
167. Hoofnagle et al., "The treatment of chronic viral hepatitis," The New England Journal of Medicine 336(5):347-356 (1997)

168. Horisberger, "MX Protein: Function and Mechanism of Action," *Interferon: Principles and Medical Applications* pp215-224 (1992)
169. Houghton et al., "Molecular Biology of the Hepatitis C Viruses: Implications for Diagnosis, Development and Control of Viral Disease," Hepatology 14(2):381-388 (1991)
170. Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," VCH, 331-417
171. Hurwitz et al., "Pharmacodynamics of (-)- β -2',3'-Dideoxy-3'-Thiacytidine in Chronically Virus-Infected Woodchucks Compared to Its Pharmacodynamics in Humans," Antimicrobial Agents and Chemotherapy 42:2804-2809 (1998)
172. Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the *let-7* Small Temporal RNA," Science 293:834-838 (2001)
173. Iacovacci et al., "Molecular Characterization and Dynamics of Hepatitis C Virus Replication in Human Fetal Hepatocytes Infected *In Vitro*," Hepatology 26(5):1328-1337 (1997)
174. Iacovacci et al., "Quantitation of hepatitis C virus RNA production in two human bone marrow-derived B-cell lines infected *in vitro*," Institut Pasteur/Elsevier 148:147-151 (1997)
175. Ilan et al., "The Hepatitis B Virus-Trimeric Mouse: A Model for Human HBV Infection and Evaluation of Anti-HBV Therapeutic Agents," Hepatology 553-562 (1999)
176. Imperial, "New Treatment Strategies in Hepatitis B and C: Natural History of Chronic Hepatitis B and C," Journal of Gastroenterology and Hepatology 14:S1-S5 (1999)
177. Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," Chem. Pharm. Bull. 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
178. Ishizaka et al., "Isolation of Active Ribozymes from an RNA Pool of Random Sequences Using an Anchored Substrate RNA," Biochemical and Biophysical Research Communication 214(2):403-409 (1995)
179. Ito et al., "Cultivation of hepatitis C virus in primary hepatocyte culture from patients with chronic hepatitis C results in release of high titre infectious virus," Journal of General Virology 77:1043-1054 (1996)

180. Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and Endogeneous Genes by Anti-Sense RNA," Science 229:345-352 (1985)
181. Jaeger et al., "Improved Predictions of Secondary Structures for RNA," Proc. Natl. Acad. Sci. USA 86:7706-7710 (1989)
182. Jarvis et al., "Optimizing the Cell Efficacy of Synthetic Ribozymes," Journal of Biological Chemistry 271:29107-29112 (1996)
183. Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," Clinical Chemistry 45:1628-1650 (1999)
184. Jeffries and Symons, "A Catalytic 13-mer Ribozyme," Nucleic Acids Research 17:1371-1377 (1989) (also referred to as Jefferies)
185. Johnson et al., "How Interferons Fight Disease," Scientific American, pp. 68-75 (May 1994)
186. Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," Fundam. Clin. Pharmacol. 13:16-26 (1999)
187. Joseph et al., "Substrate selection rules for the hairpin ribozyme determined by in vitro selection, mutation, and analysis of mismatched substrates," Genes & Development 7:130-138 (1993)
188. Joyce et al., "Amplification, mutation and selection of catalytic RNA," Gene 82:83-87 (1989)
189. Joyce, "Directed Molecular Evolution," Scientific American 267:90-97 (1992)
190. Karpeisky et al, "2'-O-Methylthiomethyl Modifications In Hammerhead Ribozymes," Nucleosides & Nucleotides 16(7-9):955-958 (1997) {Mistakenly referred to as Weifeng and Torrence}
191. Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," Tetrahedron Letters 39:1131-1134 (1998)
192. Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme," Antisense Research & Development 2:3-15 (1992)
193. Kato et al., "Molecular structure of the Japanese hepatitis C viral genome," Federation of European Biochemical Societies 280(2):325-328 (1991)

194. Kato et al., "Susceptibility of Human T-Lymphotropic Virus Type I Infected Cell Line MT-2 Hepatitis C Virus Infection¹," Biochemical and Biophysical Research Communications 206(3):863-869 (1995)
195. Kawamura et al., "Transgenic Expression of Hepatitis C Virus Structural Proteins in the Mouse," Hepatology 25(4):1014-1021 (1997)
196. Kidd et al., "A Revised Secondary Structure Model for the 3'-end of Hepatitis B Virus Pregenomic RNA," Nucleic Acids Research 24:3295-3301 (1996)
197. Kim and Cech, "Three-dimensional model of the active site of the self-splicing rRNA precursor of *Tetrahymena*," Proc. Natl. Acad. Sci. USA 84:8788-8792 (1987)
198. Kim et al., "Repression of Hepatitis B Virus X Gene Expression by Hammerhead Ribozymes," Biochemical and Biophysical Research Comm. 257:759-765 (1999)
199. Knitt et al., "pH Dependencies of the *Tetrahymena* Ribozyme Reveal an Unconventional Origin of an Apparent pK_a," Biochemistry 35:1560-1570 (1996)
200. Koike et al., "Expression of hepatitis C virus envelope proteins in transgenic mice," Journal of General Virology 76:3031-3038 (1995)
201. Kollmann et al., "The Concurrent Maturation of Mouse and Human Thymocytes in Human Fetal Thymus Implanted in NIH-beige-nude-xid Mice Is Associated with the Reconstitution of the Murine Immune System," J. Exp. Med. 177:821-832 (1993)
202. Kore, et al., "Sequence specificity of the hammerhead ribozyme revisited; the NIH rule," Nucleic Acids Research, 26(18):4116-4120 (1998)
203. Kumar and Ellington, "Artificial evolution and natural ribozymes," FASEB J. 9:1183-1195 (1995)
204. Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," Reviews in Molecular Biotechnology 74:27-38 (2000)
205. Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," Chemical Reviews 95:2601-2627 (1995)
206. Lasic and Papahadjopoulos, "Liposomes Revisited," Science 267:1275-1276 (1995)
207. Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of Macromolecules," ACS Symposium Series 752:184-192 (2000)

208. Lee and Lee, "Preparation of Cluster Glycosides of *N*-Acetylgalactosamine That Have Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific Receptor," Glycoconjugates J. 4:317-328 (1987)
209. Lee et al., "Stimulation of Natural Killer Cell Activity and Inhibition of Proliferation of Various Leukemic Cells by Purified Human Leukocyte Interferon Subtypes," Cancer Research 42:1312-1316 (1982)
210. Leinbach et al., "Substrate Specificity of the NS3 Serine Proteinase of Hepatitis C Virus as Determined by Mutagenesis at the NS3/NS4A Junction," Virology 204:163-169 (1994)
211. Leventhal et al., "Long-Term Response of Recurrent Respiratory Papillomatosis to Treatment with Lymphoblastoid Interferon Alfa-n1," The New England Journal of Medicine 325(9):613-617 (1991)
212. L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in α -Lactalbumin mRNA Levels in C1271 Mouse," EMBO J. 11:4411-4418 (1992)
213. Li and Altman, "Cleavage by RNase P of gene N mRNA reduces bacteriophage λ burst size," Nucleic Acids Research 24:835-842 (1996)
214. Li et al., "Thermodynamic and Activation Parameters for Binding of a Pyrene-Labeled Substrate by the *Tetrahymena* Ribozyme: Docking is Not Diffusion-Controlled and is Driven by a Favorable Entropy Change," Biochemistry 34:14394-14399 (1995)
215. Liang et al., "Viral Pathogenesis of Hepatocellular Carcinoma in the United States," Hepatology 18(6):1326-1333 (1993)
216. Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," Methods Enzymol. 217:47-66 (1993)
217. Lieber et al., "Elimination of Hepatitis C Virus RNA in Infected Human Hepatocytes by Adenovirus-Mediated Expression of Ribozymes," Journal of Virology 70:8782-8791 (1996)
218. Limbach et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Research 22(12):2183-2196 (1994)
219. Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," J. Am. Chem. Soc. 120:8531-8532 (1998)
220. Lisacek et al., "Automatic Identification of Group I Intron Cores in Genomic DNA Sequences," J. Mol. Biol. 235:1206-1217 (1994)

221. Lisziewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," Proc. Natl. Acad. Sci. U.S.A. 90:8000-8004 (1993)
222. Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," J. Biol. Chem. 270(42):24864-24870 (1995)
223. Lixia et al., "Blocking Effect of Hammerhead Ribozyme RCP on HBV Gene Expression in HepG2215 Cell Line," J. Med. Coll. PLA 13:157-159 (1998) [mistakenly referred to as Gan]
224. Lixia et al., "Effects of Hammerhead Ribozyme (RCP) on HBV P Gene *In Vitro*," J. Med. Coll. PLA 11:171-175 (1996) [mistakenly referred to as Gan]
225. Long and Uhlenbeck, "Kinetic characterization of intramolecular and intermolecular hammerhead RNAs with stem II deletions," Proc. Natl. Acad. Sci. USA 91:6977-6981 (1994)
226. Lu et al., "Poliovirus chimeras replicating under the translational control of genetic elements of hepatitis C virus reveal unusual properties of the internal ribosomal entry site of hepatitis C virus," Proc. Natl. Acad. Sci. USA 93:1412-1417 (1996)
227. Macejak et al., "Inhibition of Hepatitis C Virus (HCV)-RNA-Dependent Translation and Replication of a Chimeric HCV Poliovirus Using Synthetic Stabilized Ribozymes," Hepatology 31(3):769-776 (2000)
228. Maher et al., "Kinetic Analysis of Oligodeoxyribonucleotide-Directed Triple-Helix Formation on DNA," Biochemistry 29:8820-8826 (1990)
229. Marcellin et al., "Recombinant Human α -Interferon in Patients with Chronic Non-A, Non-B Hepatitis: A Multicenter Randomized Controlled Trial from France," Hepatology 13(3):393-397 (1991)
230. Marcellin et al., "Recombinant Human α -Interferon in Patients with Chronic Non-A, Non-B Hepatitis: A Multicenter Randomized Controlled Trial from France," Hepatology 13(3):393-397 (1991)
231. Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," Molecular Membrane Biology 16:129-140 (1999)
232. McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible antisense RNA," Proc. Natl. Acad. Sci. USA 83:399-403 (1986)

233. McKay, "Structure and function of the hammerhead ribozyme: an unfinished story," RNA 2:395-403 (1996)
234. Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," American Chemical Society, pp. 24-39 (1994)
235. Michel and Westhof, "Slippery substrates," Nat. Struct. Biol. 1:5-7 (1994)
236. Michel et al., "Structure and Activities of Group II Introns," Annu. Rev. Biochem. 64:435-461 (1995)
237. Michels and Pyle, "Conversion of a Group II Intron into a New Multiple-Turnover Ribozyme that Selectively Cleaves Oligonucleotides: Elucidation of Reaction Mechanism and Structure/Function Relationships," Biochemistry 34:2965-2977 (1995)
238. Milligan and Uhlenbeck, "Synthesis of Small RNAs Using T7 RNA Polymerase," Methods Enzymol. 180:51-62 (1989)
239. Milner et al., "Selecting effective antisense reagents on combinatorial oligonucleotide arrays," Nature Biotechnology 15:537-541 (1997)
240. Mitra et al., "A mammalian 2-5A system functions as an antiviral pathway in transgenic plants," Proc. Natl. Acad. Sci. USA 93:6780-6785 (1996)
241. Mizuno et al, "Virion-like Structures in HeLa G Cells Transfected with the Full-Length Sequence of the Hepatitis C Virus Genome," Gastroenterology 109:1933-1940 (1995)
242. Mizutani et al., "Characterization of Hepatitis C Virus Replication in Cloned Cells Obtained from a Human T-Cell Leukemia Virus Type 1-Infected Cell Line, MT-2," Journal of Virology 70(10):7219-7223 (1996)
243. Mizutani et al., "Long-Term Human T-Cell Culture System Supporting Hepatitis C Virus Replication," Biochemical and Biophysical Research Communications 227:822-826 (1996)
244. Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," Science 256:992-996 (1992)
245. Moriya et al., "Hepatitis C virus core protein induces hepatic steatosis in transgenic mice," Journal of General Virology 78:1527-1531 (1997)
246. Morrey et al., "Utilization of Transgenic Mice Replicating High Levels of Hepatitis B Virus for Antiviral Evaluation of Lamivudine," Antiviral Research 42:97-108 (1999)

247. Mukhopadhyay et al., "Antisense Regulation of Oncogenes in Human Cancer," Critical Reviews in Oncogenesis 7:151-190 (1996)
248. Nakajima et al., "Characterization of Long-Term Cultures of Hepatitis C Virus," Journal of Virology 70(5):3325-3329 (1996)
249. Nakamaye and Eckstein, "AUA-Cleaving Hammerhead Ribozymes: Attempted Selection for Improved Cleavage," Biochemistry 33:1271-1277 (1994)
250. Nathans and Smith, "Restriction Endonucleases in the Analysis and Restructuring of DNA Molecules," Ann. Rev. Biochem. 44:273-293 (1975)
251. Noonberg et al., *In vivo* generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation," Nucleic Acids Research 22(14):2830-2836 (1994)
252. Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell 107:309-321 (2001)
253. Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-Gun' Type Ribozyme-trimming Plasmid," Nucleic Acids Symp. Ser. 27:15-16 (1992)
254. Ohkawa et al., "Cleavage of viral RNA and inhibition of viral translation by hepatitis C virus RNA-specific hammerhead ribozyme *in vitro*," Journal of Hepatology 27:78-84 (1997)
255. Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1 Expression by a Hairpin Ribozyme," Proc. Natl. Acad. Sci. USA 89:10802-10806 (1992)
256. Okamoto et al., "Nucleotide sequence of the genomic RNA of hepatitis C virus isolated from a human carrier: comparison with reported isolates for conserved and divergent regions," Journal of General Virology 72:2697-2704 (1991)
257. Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," Biochimica et Biophysica Acta 1238:86-90 (1995)
258. Orgel, "Selection *in vitro*," Proc. R. Soc. London B. 205:435-442 (1979)
259. Ozes et al., "A Comparison of Interferon-Con1 with Natural Recombinant Interferons- α : Antiviral, Antiproliferative, and Natural Killer-Inducing Activities," Journal of Interferon Research 12:55-59 (1992)

260. Pace and Smith, "Ribonuclease P: Function and Variation," J. Biol. Chem. 265:3587-3590 (1990)
261. Pan et al., "Probing of tertiary interactions in RNA: 2'-Hydroxyl-base contacts between the RNase P and pre-tRNA," Proc. Natl. Acad. Sci. USA 92:12510-12514 (1995)
262. Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier *in vivo*," Proc. Natl. Acad. Sci. USA 92:5592-5596 (1995)
263. Pasquinelli et al., "Hepatitis C Virus Core and E2 Protein Expression in Transgenic Mice," Hepatology 25(3):719-727 (1997)
264. Passman et al., "*In Situ* Demonstration of Inhibitory Effects of Hammerhead Ribozymes that are Targeted to the Hepatitis Bx Sequence in Cultured Cells," Biochemical and Biophysical Research Communications 268:728-733 (2000)
265. Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," Nature 344:565-567 (1990) (often mistakenly listed as Perrault)
266. Perrotta and Been, "A pseudoknot-like structure required for efficient self-cleavage of hepatitis delta virus RNA," Nature 350:434-436 (1991)
267. Perrotta and Been, "Cleavage of Oligoribonucleotides by a Ribozyme Derived from the Hepatitis δ Virus RNA Sequence," Biochemistry 31:16-21 (1992)
268. Pestka et al., "Interferons and Their Actions," Ann. Rev. Biochem. 56:727-777 (1987)
269. Pestka, "[1] Interferon from 1981 to 1986," Methods in Enzymology 119:3-15 (1986)
270. Pfeffer and Strulovici, "Transmembrane Secondary Messengers for IFN α/β Interferon. *Principles and Medical Applications* 151-160 (1992)
271. Pichlmayr et al., "Indications for Liver Transplantation in Hepatobiliary Malignancy," Hepatology 20:33S-40S (1994)
272. Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," Science 253:314-317 (1991)
273. Player and Torrence, "The 2-5A System: Modulation of Viral and Cellular Processes Through Acceleration of RNA Degradation," Pharmacol Ther. 78:55-113 (1998)

274. Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and Organs," J. Med. Chem. 24:1388-1395 (1981)
275. Putlitz et al., "Combinatorial Screening and Intracellular Antiviral Activity of Hairpin Ribozymes Directed Against Hepatitis B Virus," Journal of Virology 73:5381-5387 (1999)
276. Puttaraju et al., "A circular trans-acting hepatitis delta virus ribozyme," Nucleic Acids Research 21:4253-4258 (1993)
277. Pyle et al., "Building a Kinetic Framework for Group II Intron Ribozyme Activity: Quantitation of Interdomain Binding and Reaction Rate," Biochemistry 33:2716-2725 (1994)
278. Pyle et al., "Building a Kinetic Framework for Group II Intron Ribozyme Activity: Quantitation of Interdomain Binding and Reaction Rate," Biochemistry 33:2716-2725 (1994)
279. Robertson et al., "Purification and Properties of a Specific *Escherichia coli* Ribonuclease which Cleaves a Tyrosine Transfer Ribonucleic Acid Precursor," J. Biol. Chem. 247:5243-5251 (1972)
280. Rossi et al., "Ribozymes as Anti-HIV-1 Therapeutic Agents: Principles, Applications, and Problems," Aids Research and Human Retroviruses 8:183-189 (1992)
281. Rubinstein, "Multiple Interferon Subtypes: The Phenomenon and Its Relevance," Journal of Interferon Research 7:545-551 (1987)
282. Ruiz et al., "Design and Preparation of a Multimeric Self-Cleaving Hammerhead Ribozyme," BioTechniques 22:338-345 (1997)
283. Sakamoto et al., "Intracellular Cleavage of Hepatitis C Virus RNA and Inhibition of Viral Protein Translation by Hammerhead Ribozymes," J. Clin. Invest., The American Society for Clinical Investigation, Inc. 98(12):2720-2728 (1996)
284. Samuel, "The RNA-Dependent PI/eIF-2 α Protein Kinase," *Interferon: Principles & Medical Applications* pp237-249 (1992)
285. Santoro and Joyce, "A general purpose RNA-cleaving DNA enzyme," Proc. Natl. Acad. Sci. USA 94:4262-4266 (1997)
286. Santoro et al., "Mechanism and Utility of an RNA-Cleaving DNA Enzyme," Biochemistry 37:13330-13342 (1998)

287. Santoro et al., "RNA Cleavage by a DNA Enzyme with Extended Chemical Functionality," *J. Am. Chem. Soc.* 122:2433-2439 (2000)
288. Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" *Science* 247:1222-1225 (1990)
289. Saville and Collins, "A Site-Specific Self-Cleavage Reaction Performed by a Novel RNA In *Neurospora* Mitochondria," *Cell* 61:685-696 (1990)
290. Saville and Collins, "RNA-Mediated Ligation of Self-Cleavage Products of a *Neurospora* Mitochondrial Plasmid Transcript," *Proc. Natl. Acad. Sci. USA* 88:8826-8830 (1991)
291. Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," *Proc. Natl. Acad. Sci. USA* 88:10591-10595 (1991)
292. Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β -cyanoethyl protected ribonucleoside phosphoramidites," *Nucl Acids Res.* 18:5433-5441 (1990)
293. Schmajuk et al., "Antisense Oligonucleotides with Different Backbones," *The Journal of Biological Chemistry* 274:21783-21789 (1999)
294. Schmidt et al., "Base and sugar requirements for RNA cleavage of essential nucleoside residues in internal loop B of the hairpin ribozyme: implications for secondary structure," *Nucleic Acids Research* 24:573-581 (1996)
295. Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," *Prog. Neuro-Psychopharmacol. & Biol. Psychiat.* 23:941-949 (1999) [sometimes cited by RPI as *Prog Neuropsychopharmacol Biol Psychiatry* 23:941-949, 1999]
296. Scott et al., "The crystal structure of an All-RNA hammerhead ribozyme: A proposed mechanism for RNA catalytic cleavage," *Cell* 81:991-1002 (1995)
297. Seipp et al., "Establishment of persistent hepatitis C virus infection and replication *in vitro*," *Journal of General Virology* 78:2467-2476 (1997)
298. Sells et al., "Production of Hepatitis B Virus Particles in Hep G2 Cells Transfected with Cloned Hepatitis B Virus DNA," *Proc. Natl. Acad. Sci.* 84:1005-1009 (1987)
299. Shabarova et al., "Chemical ligation of DNA: The first non-enzymatic assembly of a biologically active gene," *Nucleic Acids Research* 19:4247-4251 (1991)

300. Sherlock, "Viral hepatitis," The Lancet 339:802 (1992)
301. Silverman et al., "Selective RNA Cleavage by Isolated RNase L Activated with 2-5A Antisense Chimeric Oligonucleotides," Methods in Enzymology 313:522-533 (1999)
302. Simmonds et al., "Identification of genotypes of hepatitis C virus by sequence comparisons in the core, E1 and NS-5 regions," Journal of General Virology 75:1053-1061 (1994)
303. Simmonds, "Variability of Hepatitis C Virus," Hepatology 21:570-583 (1995)
304. Smith and Simmonds, "Characteristics of Nucleotide Substitution in the Hepatitis C Virus Genome: Constraints on Sequence Change in Coding Regions at Both Ends of the Genome," J. Mol. Evol. 45:238-246 (1997)
305. Stein and Cheng, "Antisense Oligonucleotides as Therapeutic Agents - Is the Bullet Really Magical?" Science 261:1004-1288 (1993)
306. Stein et al., "A Specificity Comparison of Four Antisense Types: Morpholino, 2'-O-Methyl RNA, DNA, and Phosphorothioate DNA," Antisense & Nucleic Acid Drug Development 7:151-157 (1997)
307. Strobel and Dervan, "Site-Specific Cleavage of a Yeast Chromosome by Oligonucleotide-Directed Triple-Helix Formation," Science 249:73-75 (1990)
308. Strobel et al., "Exocyclic Amine of the Conserved G-U Pair at the Cleavage Site of the *Tetrahymena* Ribozyme Contributes to 5'-Splice Site Selection and Transition State Stabilization," Biochemistry 35:1201-1211 (1996)
309. Strobel et al., "Minor Groove Recognition of the Conserved G-U Pair at the *Tetrahymena* Ribozyme Reaction Site," Science 267:675-679 (1995)
310. Sullenger and Cech, "Ribozyme-mediated repair of defective mRNA by targeted trans-splicing," Nature 371:619-622 (1994)
311. Sullenger and Cech, "Tethering Ribozymes to a Retroviral Packaging Signal for Destruction of Viral RNA," Science 262:1566-1569 (1993)
312. Sullenger et al., "Overexpression of TAR Sequences Renders Cells Resistant to Human Immunodeficiency Virus Replication," Cell 63:601-608 (1990)
313. Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," Current Opinion in Molecular Therapeutics 2:100-105 (2000)
314. Symons, "Ribozymes," Current Opinion in Structural Biology 4(3):322-330 (1994)

315. Szostak, "In Vitro Genes," TIBS 17:89-93 (1993)
316. Tagawa et al., "Infection of human hepatocyte cell lines with hepatitis C virus *in vitro*," Journal of Gastroenterology and Hepatology 10:523-527 (1995)
317. Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be used both *in vitro* in place of run-off and (G)-free transcriptions and *in vivo* as multi-sequences transcription vectors," Nucleic Acids Research 19:5125-5130 (1991)
318. Takahashi et al., "Natural Course of Chronic Hepatitis C," The American Journal of Gastroenterology 88(2):240-243 (1993)
319. Takehara et al., "Expression of the Hepatitis C Virus Genome in Rat Liver After Cationic Liposome-Mediated *In Vivo* Gene Transfer," Hepatology 21:746-751 (1995)
320. Tang et al., "Examination of the catalytic fitness of the hammerhead ribozyme by *in vitro* selection," RNA 3:914-925 (1997)
321. Thompson et al., "Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter," Nucleic Acids Research 23:2259-2268 (1995)
322. Tong et al., "Evidence for Hepatitis C Viral Infection in Patients With Primary Hepatocellular Carcinoma," West J Med 160:133-138 (1994)
323. Tong et al., "Prediction of Response During Interferon Alfa 2b Therapy in Chronic Hepatitis C Patients Using Viral and Biochemical Characteristics: A Comparison," Hepatology 26(6):1640-1645 (1997)
324. Tong et al., "Treatment of Chronic Hepatitis C With Consensus Interferon: A Multicenter, Randomized, Controlled Trial," Hepatology 26(3):747-754 (1997)
325. Torrence et al., "Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense chimera," Proc. Natl. Acad. Sci. USA 90:1300-1304 (1993)
326. Trinchet et al., "Carcinome Hépatocellulaire: Traitement par Chimioembolisation Artérielle," Presse Med 23(18):831-3 (1994)
327. Turner et al., "Improved Parameters for Prediction of RNA Structure," Cold Spring Harbor Symposia on Quantitative Biology Volume LII, pp. 123-133 (1987)
328. Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," J. Am. Chem. Soc. 109:3783-3785 (1987)

329. Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," *Proc. Natl. Acad. Sci. USA* 96:7053-7058 (1999)
330. Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter neuronal cells in vivo," *FEBS Letters* 421:280-284 (1998)
331. Uhlenbeck, "A Small Catalytic Oligoribonucleotide," *Nature* 328:596-600 (1987)
332. Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle," *Chemical Reviews* 90:544-584 (1990)
333. Usman and Cedergren, "Exploiting the chemical synthesis of RNA," *TIBS* 17:334-339 (1992)
334. Usman and McSwiggen, "Ch. 30 - Catalytic RNA (Ribozymes) as Drugs," *Annual Reports in Medicinal Chemistry* 30:285-294 (1995)
335. Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an *Escherichia coli* Formylmethionine tRNA," *J. Am. Chem. Soc.* 109:7845-7854 (1987)
336. Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," *Nucleic Acids Symposium Series* 31:163-164 (1994)
337. Usman et al., "Hammerhead ribozyme engineering," *Current Opinion in Structural Biology* 1:527-533(1996)
338. Vaish et al., "Isolation of Hammerhead Ribozymes with Altered Core Sequences by *in Vitro* Selection," *Biochemistry* 36:6495-6501 (1997)
339. Valli et al., "Detection of a 5' UTR variation in the HCV genome after long-term *in vitro* infection," *Institut Pasteur/Elsevier* 146:285-288 (1995)
340. Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," *Nucleic Acids Research* 21:3249-3255 (1993)
341. Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," *Annu. Rev. Biochem.* 67:99-134 (1998)
342. Wands et al., "Nucleic Acid-based Antiviral and Gene Therapy of Chronic Hepatitis B Infection," *Jour. of Gastroenterology and Hepatology* 12:S354-S369 (1997)

343. Wang et al., "Translation of Human Hepatitis C Virus RNA in Cultured Cells Is Mediated by an Internal Ribosome-Binding Mechanism," Journal of Virology 67(6):3338-3344 (1993)
344. Warashina, et al., "Extremely High and Specific Activity of DNA Enzymes in Cells with a Philadelphia Chromosome, Chemistry & Biology, 6(4):237-250 (1999)
345. Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4⁺ Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," Journal of Virology 65:5531-5534 (1994)
346. Welch et al., "A potential therapeutic application of hairpin ribozymes: *in vitro* and *in vivo* studies of gene therapy for hepatitis C virus infection," Gene Therapy 3:994-1001 (1996)
347. Welch et al., "Intracellular Application of Hairpin Ribozyme Genes Against Hepatitis B Virus," Gene Therapy 4:736-743 (1997)
348. Werner and Uhlenbeck, "The effect of base mismatches in the substrate recognition helices of hammerhead ribozymes on binding and catalysis," Nucleic Acids Research 23:2092-2096 (1995)
349. Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," Nature Cell Biology 2:70-75 (2000)
350. Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," Nucleic Acids Research 23(14):2677-2684 (1995)
351. Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," Methods in Molecular Biology 74:59-69 (1997)
352. Woolf et al., "Specificity of Antisense Oligonucleotides *in vivo*," Proc. Natl. Acad. Sci. USA 89:7305-7309 (1992)
353. Wu and Wu, "Receptor-mediated *in Vitro* Gene Transformation by a Soluble DNA Carrier System," The Journ. of Biol. Chem. 262:4429-4432 (1987)
354. Wu-Pong, "Oligonucleotides: Opportunities for Drug Therapy and Research," BioPharm pp20-33 (1994)
355. Yamamoto et al., "*In Vivo* Transfection of Hepatitis C Virus Complementary DNA Into Rodent Liver by Asialoglycoprotein Receptor Mediated Gene Delivery," Hepatology 22(3):847-855 (1995)

356. Yoo et al., "Transfection of a Differentiated Human Hepatoma Cell Line (Huh7) with In Vitro-Transcribed Hepatitis C Virus (HCV) RNA and Establishment of a Long-Term Culture Persistently Infected with HCV," Journal of Virology 69(1):32-38 (1995)
357. Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," Proc. Natl. Acad. Sci. USA 90:6340-6344 (1993)
358. Yuan et al., "Targeted cleavage of mRNA by human RNase P," Proc. Natl. Acad. Sci. USA 89:8006-8010 (1992)
359. Zarrinkar and Williamson, "The P9.1-P9.2 peripheral extension helps guide folding of the *Tetrahymena* ribozyme," Nucleic Acids Research 24:854-858 (1996)
360. Zaug et al., "The *Tetrahymena* Ribozyme Acts Like an RNA Restriction Endonuclease," Nature 324:429-433 (1986)
361. Zhiqiang et al., "*In Vivo* Inhibition of Hepatitis B Viral Gene Expression by Antisense Phosphorothioate Oligodeoxynucleotides in Athymic Nude Mice," Journal of Viral Hepatitis 3:19-22 (1996) [mistakenly referred to as Yao]
362. Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," Mol. Cell. Biol. 10:4529-4537 (1990)
363. Zimmerly et al., "A Group II Intron RNA is a Catalytic Component of a DNA Endonuclease Involved in Intron Mobility," Cell 83:529-538 (1995)
364. Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent $\alpha 1(I)$ Collagen by a Homologous Transcriptionally Self-Silenced Transgene," Molecular and Cellular Biology, 19:274-283 (1999)
365. Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," Science, 286, 950-952 (1999)
366. International Search Report for PCT/US03/05043 mailed January 16, 2004
367. McCaffrey et al., "RNA interference in adult mice," Nature, 418, 38-39 (2002)
368. Randall et al., "Clearance of replicating hepatitis C virus replicon RNAs in cell culture by small interfering RNAs," PNAS, 100:1, 235-240 (2003)
369. Lin et al., "Policing rogue genes," Nature, 402, 128-129 (1999)
370. Sharp et al., "RNAi and double-strand RNA," Genes & Development, 13:139-141 (1999)


371. Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found," Molecular Biology, Vol. 286, No. 5441, p. 886 (1999) [sometimes mistakenly referred to as being published in Science]
372. Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," Genes & Development 13:3191-3197 (1999)
373. Waterhouse et al., "Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA," Proc. Natl. Acad. Sci. USA, 95, 13959-13964 (1998)

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff

Date: August 3, 2004

By:



Anita J. Terpstra
Reg. No. 47,132

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive, 32nd Floor
Chicago, IL 60606
Telephone: 312-913-0001
Facsimile: 312-913-0002

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office



INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

U.S. PATENT APPLICATION DOCUMENTS

Examiner Initial		Document Number	Filing Date	Name	Class	Subclass	Publication Date if Appropriate
	*	07/882,712	05/14/92	Draper et al.			
	*	08/193,627	02/07/94	Draper et al.			
	*	08/878,640	06/19/97	Ludwig et al.			
	*	09/205,520	12/03/98	Sullenger et al.			
	*	09/257,553	02/24/99	Blatt et al.			
	*	09/274,553	03/23/99	Blatt et al.			
	*	09/436,430	11/09/99	Draper et al.			
	*	09/476,387	12/30/99	Beigelman et al.			
	*	09/504,321	02/15/00	Blatt et al.			
	*	09/531,025	03/20/00	Draper et al.			
	*	09/611,931	07/07/00	Blatt et al.			
	*	09/636,385	08/09/00	Draper et al.			
	*	09/696,347	10/24/00	Draper et al.			
	*	09/740,332	12/18/00	Blatt et al.			
	*	09/817,879	03/26/01	Blatt et al.			
	*	09/877,478	06/08/01	Draper et al.			

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	*	09/877,526	06/08/01	Usman et al.			
	*	09/918,728	07/31/01	Beigelman et al.			
	*	60/082,404	04/20/98	Thompson et al.			
	*	60/083,217	04/27/98	McSwiggen et al.			
	*	60/100,842	09/18/98	Blatt et al.			
	*	60/101,174	09/21/98	Hartmann et al.			
	*	60/296,876	06/08/01	Macejak et al.			
	*	60/337,055	12/05/01	Morrissey et al.			
	*	60/355,059	10/24/01	Macejak et al.			
	*	60/358,580	02/20/02	Beigelman et al.			
	*	60/363,124	03/11/02	Beigelman et al.			

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	*	4,859,768	08/22/89	Suhadolnik et al.			
	*	4,924,624	05/15/90	Suhadolnik et al.			
	*	4,987,071	01/22/91	Cech et al.			
	*	5,188,897	02/23/93	Suhadolnik et al.			

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	*	5,334,711	08/22/94	Sproat			
	*	5,405,939	04/11/95	Suhadolnik et al.			
	*	5,475,096	12/12/95	Gold et al.			
	*	5,525,468	06/11/96	McSwiggen et al.			
	*	5,550,111	08/27/96	Suhadolnik et al.			
	*	5,556,840	09/17/96	Suhadolnik et al.			
	*	5,567,588	10/22/96	Gold et al.			
	*	5,583,032	12/10/96	Torrence et al.			
	*	5,589,332	12/31/96	Shih et al.			
	*	5,610,054	03/11/97	Draper et al.			
	*	5,624,803	04/29/97	Noonberg et al.			
	*	5,625,047	04/29/97	Been et al.			
	*	5,627,053	05/06/97	Usman et al.			
	*	5,631,359	05/20/97	Chowrira & McSwiggen			
	*	5,633,133	05/27/97	Long et al.			
	*	5,643,889	07/01/97	Suhadolnik et al.			
	*	5,670,633	09/23/97	Cook et al.			
	*	5,672,695	09/30/97	Eckstein et al.			
	*	5,700,785	12/23/97	Suhadolnik et al.			

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	*	5,716,824	02/10/98	Beigelman et al.			
	*	5,741,679	04/21/98	George et al.			
	*	5,792,847	08/11/98	Buhr et al.			
	*	5,807,718	09/15/98	Joyce et al.			
	*	5,817,796	10/06/98	Stinchcomb et al.			
	*	5,834,186	11/10/98	George et al.			
	*	5,849,902	12/15/98	Arrow et al.			
	*	5,854,038	12/29/98	Sullenger and Cech			
	*	5,859,226	01/12/99	Hunt et al.			
	*	5,863,905	01/26/99	Suhadolnik et al.			
	*	5,869,253	02/09/99	Draper et al.			
	*	5,871,914	02/16/99	Nathan et al.			
	*	5,898,031	04/27/99	Crooke			
	*	5,962,431	10/05/99	Budowsky et al.			
	*	5,989,912	11/23/99	Arrow et al.			
	*	6,001,311	12/14/99	Brennan			
	*	6,005,087	12/21/99	Cook et al.			
	*	6,017,756	01/25/00	Draper et al.			
	*	6,107,094	08/22/00	Crooke			

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	*	6,127,173	12/03/00	Eckstein et al.			
	*	6,159,714	12/12/00	Usman et al.			
	*	6,300,074	10/09/01	Gold et al.			
	*	6,476,205	11/05/02	Buhr et al.			

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	1.	EP 0 360 257	03/28/90	EP (Hampel et al.)				
	2.	JP 07231784		JP (Yamada et al.)				
	3.	PCT/US02/09187	03/26/02	WO (Beigelman et al.)				
	4.	WO 91/03162	03/21/91	WO (Rossi et al.)				
	5.	WO 92/07065	04/30/92	WO (Eckstein et al.)				
	6.	WO 93/15187	08/05/93	WO (Usman et al.)				
	7.	WO 93/23057	11/25/93	WO (Sullivan et al.)				
	8.	WO 93/23569	11/25/93	WO (Draper et al.)				
	9.	WO 94/02595	02/03/94	WO (Sullivan et al.)				
	10.	WO 95/04818	02/16/95	WO (Draper et al.)				
	11.	WO 95/11304	04/27/95	WO (Usman et al.)				

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	12.	WO 95/13380	04/27/95	WO (Draper et al.)				
	13.	WO 95/22600	08/24/95	WO (Goldenberg et al.)				
	14.	WO 95/23225	08/31/95	WO (Stinchcomb et al.)				
	15.	WO 96/10390	04/11/96	WO (Ansell et al.)				
	16.	WO 96/10391	04/11/96	WO (Choi et al.)				
	17.	WO 96/10392	04/11/96	WO (Holland et al.)				
	18.	WO 96/18419	06/20/96	WO (Kay et al.)				
	19.	WO 96/18736	06/20/96	WO (Beigelman et al.)				
	20.	WO 96/19577	06/27/96	WO (Collins et al.)				
	21.	WO 96/22689	08/01/96	WO (Pyle et al.)				
	22.	WO 97/08309	03/06/97	WO (Goldenberg et al.)				
	23.	WO 97/26270	07/24/97	WO (Wincott et al.)				
	24.	WO 97/32018	09/04/97	WO (Barber et al.)				
	25.	WO 98/13526	04/02/98	WO (Woolf et al.)				
	26.	WO 98/27104	06/25/98	WO (Breaker et al.)				
	27.	WO 98/28317	07/02/98	WO (Karpeisky et al.)				
	28.	WO 98/43993	10/08/98	WO (Breaker et al.)				
	29.	WO 98/58058	12/23/98	WO (Ludwig et al.)				
	30.	WO 99/07409	02/18/99	WO (Deschamps de Paillette)				

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	31.	WO 99/14226	03/25/99	WO (Wengel et al.)				
	32.	WO 99/16307	04/08/99	WO (Vierling)				
	33.	WO 99/16871	04/08/99	WO (Eckstein et al.)				
	34.	WO 99/20641	04/29/99	WO (Lu)				
	35.	WO 99/29842	06/17/99	WO (Sullenger et al.)				
	36.	WO 99/31262	06/24/99	WO (Barry et al.)				
	37.	WO 99/32619	07/01/99	WO (Fire et al.)				
	374.	WO 99/49029	09/30/99	WO (Graham et al.)				
	375.	WO 99/53050	10/21/99	WO (Waterhouse et al.)				
	38.	WO 99/54459	10/28/99	WO (Thompson et al.)				
	39.	WO 99/55857	11/04/99	WO (Beigelman et al.)				
	376.	WO 99/61631	12/02/99	WO (Heifetz et al.)				
	40.	WO 00/01846	01/13/00	WO (Plaetinck et al.)				
	41.	WO 00/04141	01/27/00	WO (Kao et al.)				
	42.	WO 00/14219	03/16/00	WO (Torrence et al.)				
	43.	WO 00/24931	05/04/00	WO (Nathan and Ellington)				
	44.	WO 00/26226	05/11/00	WO (Breaker et al.)				
	45.	WO 00/44895	08/03/00	WO (Kreutzer et al.)				
	46.	WO 00/44914	08/03/00	WO (Li et al.)				

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

	47.	WO 00/53722	09/14/00	WO (O'Hare and Normand)				
	377.	WO 00/63364	10/26/00	WO (Pachuk et al.)				
	48.	WO 00/66604	11/09/00	WO (Wengel et al.)				
	49.	WO 01/29058	10/13/01	WO (Mello and Fire)				
	50.	WO 01/36646	05/25/01	WO (Zernicka-Goetz et al.)				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

	51.	Abramovitz et al., "Catalytic Role of 2'-Hydroxyl Groups Within a Group II Intron Active Site," <u>Science</u> 271:1410-1413 (1996)
	52.	Akhtar and Juliano, "Cellular Uptake and Intracellular Fate of AntiSense Oligonucleotides," <u>Trends Cell Biol.</u> 2:139-144 (1992)
	53.	Aldrian-Herrada et al., "A peptide nucleic acid (PNA) is more rapidly internalized in cultured neurons when coupled to a <i>retro-inverso</i> delivery peptide. The antisense activity depresses the target mRNA and protein in magnocellular oxytocin neurons," <u>Nucleic Acids Research</u> 26:4910-4916 (1998)
	54.	Alter, "Chronic Consequences of Non-A, Non-B Hepatitis," <i>Current Perspectives in Hepatology</i> , pp. 83-89 (1989)
	55.	Baenziger and Fiete, "Galactose and N-Acetylgalactosamine-Specific Endocytosis of Glycopeptides by Isolated Rat Hepatocytes," <u>Cell</u> 22:611-620 (1980)
	56.	Banerjee and Turner, "The Time Dependence of Chemical Modification Reveals Slow Steps in the Folding of a Group I Ribozyme," <u>Biochemistry</u> 34:6504-6512 (1995)
	57.	Bartel and Szostak, "Isolation of New Ribozymes from a Large Pool of Random Sequences," <u>Science</u> 261:1411-1418 (1993)
	58.	Bass, "The short answer," <i>Nature</i> 411:428-429 (2001)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		Applicant: Beigelman et al.	
		Filing Date: September 23, 2003	Group: 1632

59.	Beaucage and Iyer, "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives," <u>Tetrahedron</u> 49:1925-1963 (1993)
60.	Beaudry and Joyce, "Directed Evolution of an RNA Enzyme," <u>Science</u> 257:635-641 (1992)
61.	Beck and Nassal, "Efficient hammerhead ribozyme-mediated cleavage of the structured hepatitis B virus encapsidation signal <i>in vitro</i> and in cell extracts, but not in intact cells," <u>Nucleic Acids Res.</u> , 23(24), 4954-62 (1995)
62.	Beigelman et al., "Chemical Modification of Hammerhead Ribozymes," <u>The Journal of Biological Chemistry</u> 270:25702-25708 (1995)
63.	Bellon et al., "Amino-Linked Ribozymes: Post-Synthetic Conjugation of Half-Ribozymes," <u>Nucleosides & Nucleotides</u> 16:951-954 (1997)
64.	Bellon et al., "Post-synthetically Ligated Ribozymes: An Alternative Approach to Iterative Solid Phase Synthesis," <u>Bioconjugate Chem.</u> 8:204-212 (1997)
65.	Bernstein et al., "Role for a Bidentate Ribonuclease in the Initiation Step of RNA Interference," <u>Nature</u> 409:363-366 (2001)
66.	Berzal-Herranz et al., "Essential nucleotide sequences and secondary structure elements of the hairpin ribozyme," <u>EMBO J.</u> 12:2567-2574 (1993)
67.	Berzal-Herranz et al., "In vitro selection of active hairpin ribozymes by sequential RNA-catalyzed cleavage and ligation reactions," <u>Genes & Development</u> 6:129-134 (1992)
68.	Bevilacqua et al., "A Mechanistic Framework for the Second Step of Splicing Catalyzed by the <i>Tetrahymena</i> Ribozyme," <u>Biochemistry</u> 35:648-568 (1996)
69.	Boado et al., "Drug Delivery of Antisense Molecules to the Brain for Treatment of Alzheimer's Disease and Cerebral AIDS," <u>Journal of Pharmaceutical Sciences</u> 87:1308-1315 (1998)
70.	Boado, "Antisense drug delivery through the blood-brain barrier," <u>Advanced Drug Delivery Reviews</u> 15:73-107 (1995)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

71.	Bock et al., "The Enhancer I Core Region Contributes to the Replication Level of Hepatitis B Virus In Vivo and In Vitro," <u>Jour. of Virology</u> 74:2193-2202 (2000)
72.	Borden, "Interferons—Expanding Therapeutic Roles," <u>The New England Journal of Medicine</u> 326(22):1491-1493 (1992)
73.	Breaker and Joyce, "Inventing and improving ribozyme function: rational design versus iterative selection methods," <u>TIBTECH</u> 12:268-275 (1994)
74.	Breaker et al., "A DNA enzyme with Mg ²⁺ -dependent RNA phosphoesterase activity," <u>Chemistry & Biology</u> 2(10):655-660 (1995)
75.	Breaker, "Are engineered proteins getting competition from RNA?" <u>Current Opinion in Biotechnology</u> 7:442-448 (1996)
76.	Breaker, "Catalytic DNA: in training and seeking employment," <u>Nature Biotechnology</u> 17:422-423 (1999)
77.	Brennan et al., "Two-Dimensional Parallel Array Technology as a New Approach to Automated Combinatorial Solid-Phase Organic Synthesis," <u>Biotechnology and Bioengineering (Combinatorial Chemistry)</u> 61:33-45 (1998)
78.	Brody and Gold, "Aptamers as therapeutic and diagnostic agents," <u>Reviews in Molecular Biotechnology</u> 74:5-13 (2000)
79.	Brown et al., "Secondary structure of the 5' nontranslated regions of hepatitis C virus and pestivirus genomic RNAs," <u>Nucleic Acids Research</u> 20:5041-5045 (1992)
80.	Burgin et al., "Chemically Modified Hammerhead Ribozymes with Improved Catalytic Rates," <u>Biochemistry</u> 35:14090-14097 (1996) (volume no. mistakenly listed as 6)
81.	Burke et al., "Structural Analysis and Modifications of the Hairpin Ribozyme," <u>Nucleic Acids and Molecular Biology</u> , edited by Eckstein and Lilley, Springer-Verlag Berlin Heidelberg, 10:129-143 (1996)
82.	Burlina et al., "Chemical Engineering of RNase Resistant and Catalytically Active Hammerhead Ribozymes," <u>Bioorganic & Medicinal Chemistry</u> 5:1999-2010 (1997)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Applicant: Beigelman et al.	
		Filing Date: September 23, 2003	Group: 1632
		(Use several sheets if necessary)	

83.	Caruthers et al., "Chemical Synthesis of Deoxyoligonucleotides and Deoxyoligonucleotide Analogs," <u>Methods in Enzymology</u> 211:3-19 (1992)
84.	Cech et al., "Representation of the secondary and tertiary structure of group I introns," <u>Nature Structural Biology</u> 1:273-280 (1994)
85.	Cech, "Ribozymes and Their Medical Implications," <u>JAMA</u> 260:3030-3034 (1988)
86.	Chartrand et al., "An oligodeoxyribonucleotide that supports catalytic activity in the hammerhead ribozyme domain," <u>Nucleic Acids Research</u> 23(20):4092-4096 (1995)
87.	Charubala and Pfeleiderer, "Chemical Synthesis of 2',5'-Oligoadenylate Analogues," <u>Progress in Molecular and Subcellular Biology</u> 14:114-138 (1994)
88.	Chebath & Revel, "The 2-5 A System: 2-5 A Synthetases, Isospecies and Functions," <u>Interferon: Principles and Medical Applications</u> pp225-236 (1992)
89.	Chen et al., "Multitarget-Ribozyme Directed to Cleave at up to Nine Highly Conserved HIV-1 env RNA Regions Inhibits HIV-1 Replication-Potential Effectiveness Against Most Presently Sequenced HIV-1 Isolates," <u>Nucleic Acids Research</u> 20:4581-4589 (1992)
90.	Chen et al., "Probing Immune Functions in RAG-deficient Mice," <u>Current Biology</u> 6:313-319 (1994)
91.	Choo et al., "Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome," <u>Science</u> 244:359-362 (1989)
92.	Chowrira et al., "In Vitro and in Vivo Comparison of Hammerhead, Hairpin, and Hepatitis Delta Virus Self-Processing Ribozyme Cassettes," <u>J. Biol. Chem.</u> 269:25856-25864 (1994)
93.	Chowrira et al., "Novel guanosine requirement for catalysis by the hairpin ribozyme," <u>Nature</u> 354:320-322 (1991)
94.	Christoffersen and Marr, "Ribozymes as Human Therapeutic Agents," <u>J. Med. Chem.</u> 38:2023-2037 (1995) (also referred to as Christofferson and Marr)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

95.	Christoffersen et al., "Application of computational technologies to ribozyme biotechnology products," <u>Journal of Molecular Structure (Theochem)</u> 311:273-284 (1994) (maybe referred to as Christofferson)
98.	Colacino and Staschke, "The Identification and Development of Antiviral Agents...", <u>Progress in Drug Research</u> 50:259-322 (1998)
97.	Collins and Olive, "Reaction Conditions and Kinetics of Self-Cleavage of a Ribozyme Derived From <i>Neurospora</i> VS RNA," <u>Biochemistry</u> 32:2795-2799 (1993)
98.	Connolly et al., "Binding and Endocytosis of Cluster Glycosides by Rabbit Hepatocytes," <u>The Journ. of Biol. Chem.</u> 257:939-945 (1982)
99.	Conry et al., "Phase I Trial of a Recombinant Vaccinia Virus Encoding Carcinoembryonic Antigen in Metastatic Adenocarcinoma: Comparison of Intradermal versus Subcutaneous Administration," <u>Clinical Cancer Research</u> 5:2330-2337 (1999)
100.	Couture and Stinchcomb, "Anti-gene therapy: the use of ribozymes to inhibit gene function," <u>Trends In Genetics</u> 12:510-515 (1996)
101.	Cribier et al., " <i>In vitro</i> infection of peripheral blood mononuclear cells by hepatitis C virus," <u>Journal of General Virology</u> 76:2485-2491 (1995)
102.	Crooke, "Advances in Understanding the Pharmacological Properties of Antisense Oligonucleotides," <u>Advances in Pharmacology</u> 40:1-49 (1997)
103.	Crooke, "Antisense Therapeutics," <u>Biotechnology and Genetic Engineering Reviews</u> 15:121-157 (1998)
104.	Crooke, "Progress in Antisense Technology: The End of the Beginning," <u>Methods in Enzymology</u> 313:3-45 (1999)
105.	D'Amico et al., "Survival and Prognostic Indicators in Compensated and Decompensated Cirrhosis," <u>Digestive Diseases and Sciences</u> 31(5):468-475 (1986)
106.	Daniels et al., "Two Competing Pathways for Self-splicing by Group II Introns: A Quantitative Analysis of <i>in Vitro</i> Reaction Rates and Products," <u>J. Mol. Biol.</u> 256:31-49 (1996)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Applicant: Beigelman et al.	
		Filing Date: September 23, 2003	Group: 1632
(Use several sheets if necessary)			

107.	Dash et al., "Transfection of HepG2 Cells with Infectious Hepatitis C Virus Genome," <u>American Journal of Pathology</u> 151(2):363-373 (1997)
108.	Davis and Lim, "Current Status of Interferon Therapy for Chronic Hepatitis C: A Hepatologist's Perspective," <u>Infectious Agents and Disease</u> 2:150-154 (1993)
109.	Davis et al., "Treatment of Chronic Hepatitis C with Recombinant Interferon Alfa," <u>The New England Journal of Medicine</u> 321(22):1501-1506 (1989)
110.	Delihias et al., "Natural antisense RNA/target RNA interactions: Possible models for antisense oligonucleotide drug design," <u>Nature Biotechnology</u> 15:751-753 (1997)
111.	Diaz et al., "Structure of the Human Type-I Interferon Gene Cluster Determined from a YAC Clone Contig," <u>Genomics</u> 22:540-552 (1994)
112.	Doherty and Doudna, "Ribozyme Structures and Mechanisms," <u>Annu. Rev. Biophys. Biomol. Struct.</u> 30:457-475 (2001)
113.	Dreyfus, "Restriction Ribozymes?" <u>Einstein Quarterly Journal of Biology and Medicine</u> 6:92-93 (1988)
114.	Dropulic et al., "Functional Characterization of a U5 Ribozyme: Intracellular Suppression of Human Immunodeficiency Virus Type I Expression," <u>Journal of Virology</u> 66:1432-1441 (1992)
115.	Dusheiko et al., "Sequence variability of hepatitis C virus and its clinical relevance," <u>Journal of Viral Hepatitis</u> 1:3-15 (1994)
116.	Duval-Valentin, "Specific inhibition of transcription by triple helix-forming oligonucleotides," <u>Proc. Natl. Acad. Sci. USA</u> 89:504-508 (1992)
117.	Earnshaw et al., "Modified Oligoribonucleotides as Site-Specific Probes of RNA Structure and Function," <u>Biopolymers</u> 48:39-55 (1998)
118.	Egholm et al., "PNA hybridizes to complementary oligonucleotides obeying the Watson-Crick hydrogen-bonding rules," <u>Nature</u> 365:566-568 (1993)
119.	Elbashir et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," <u>Nature</u> 411:494-498 (2001)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

120.	Elbashir et al., "Functional Anatomy of siRNAs for Mediating Efficient RNAi in <i>Drosophila Melanogaster</i> Embryo Lysate," <u>The EMBO Journal</u> 20:6877-6888 (2001)
121.	Elbashir et al., "RNA Interference is Mediated by 21- and 22-Nucleotide RNAs," <u>Genes and Development</u> 15:188-200 (2001)
122.	Elkins and Rossi, "Ch. 2 - Cellular Delivery of Ribozymes," in <u>Delivery Strategies for Antisense Oligonucleotide Therapeutics</u> , edited by Akhtar, CRC Press, pp. 17-220 (1995)
123.	Elroy-Stein and Moss, "Cytoplasmic Expression System Based on Constitutive Synthesis of Bacteriophage T7 RNA Polymerase in Mammalian Cells," <u>Proc. Natl. Acad. Sci. USA</u> 87:6743-6747 (1990)
124.	Emerich et al., "Biocompatibility of Poly (DL-Lactide-co-Glycolide) Microspheres Implanted Into the Brain," <u>Cell Transplantation</u> 8:47-58 (1999)
125.	Farci et al., "A Long-Term Study of Hepatitis C Virus Replication in Non-A, Non-B Hepatitis," <u>The New England Journal of Medicine</u> 325(2):98-104 (1991)
126.	Feldstein et al., "Two sequences participating in the autolytic processing of satellite tobacco ringspot virus complementary RNA," <u>Gene</u> 82:53-61 (1989)
127.	Fire et al., "Potent and Specific Genetic Interference by Double-Stranded RNA in <i>Caenorhabditis Elegans</i> ," <u>Nature</u> 391:806-811(1998)
128.	Fire, "RNA-triggered Gene Silencing," <u>TIG</u> 15:358-363(1999)
129.	Fish et al., "The Role of Three Domains in the Biological Activity of Human Interferon- α ," <u>Journal of Interferon Research</u> 9:97-114 (1989)
130.	Forster and Altman, "External Guide Sequences for an RNA Enzyme," <u>Science</u> 249:783-786 (1990)
131.	Freier et al., "Improved free-energy parameters for predictions of RNA duplex stability," <u>Proc. Natl. Acad. Sci. USA</u> 83:9373-9377 (1986) [sometimes referred to as Frier]
132.	Galun et al., "Hepatitis C Virus Viremia in SCID \rightarrow BNX Mouse Chimera," <u>The Journal of Infectious Diseases</u> 172:25-30 (1995)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

133.	Gao and Huang, "Cytoplasmic Expression of a Reporter Gene by Co-Delivery of T7 RNA Polymerase and T7 Promoter Sequence with Cationic Liposomes," <u>Nucleic Acids Research</u> 21:2867-2872 (1993)
134.	Genbank Accession No. AF100308.1
135.	Genbank Accession No. D11168
136.	Genbank Accession No. D50483.1
137.	Genbank Accession No. L38318
138.	Genbank Accession No. S82227
139.	Gold et al., "Diversity of Oligonucleotide Functions," <u>Annu. Rev. Biochem.</u> 64:763-797 (1995)
140.	Good et al., "Expression of small, therapeutic RNAs in human nuclei," <u>Gene Therapy</u> 4:45-54 (1997)
141.	Grasby et al., "Purine Functional Groups in Essential Residues of the Hairpin Ribozyme Required for Catalytic Cleavage of RNA," <u>Biochemistry</u> 34:4068-4076 (1995)
142.	Griffin et al., "Group II intron ribozymes that cleave DNA and RNA linkages with similar efficiency, and lack contacts with substrate 2'-hydroxyl groups," <u>Chemistry & Biology</u> 2:761-770 (1995)
143.	Griffin et al., "Group II intron ribozymes that cleave DNA and RNA linkages with similar efficiency, and lack contacts with substrate 2'-hydroxyl groups," <u>Chemistry & Biology</u> 2:761-770 (1995)
144.	Guerrier-Takada et al., "The RNA Moiety of Ribonuclease P Is the Catalytic Subunit of the Enzyme," <u>Cell</u> 35:849-857 (1983)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

145.	Guidos et al., "Development of CD4 ⁺ CD8 ⁺ Thymocytes in RAG-deficient Mice Through a T Cell Receptor β Chain-independent Pathway," <u>J. Exp. Med.</u> 181:1187-1195 (1995) [mistakenly referred to as Guidas]
146.	Guidotti et al., "High-Level Hepatitis B Virus Replication in Transgenic Mice," <u>Journal of Virology</u> 69:6158-6169 (1995)
147.	Guo and Collins, "Efficient <i>trans</i> -cleavage of a stem-loop RNA substrate by a ribozyme derived from <i>Neurospora</i> VS RNA," <u>EMBO J.</u> 14:368-376 (1995)
148.	Hall, "Monoclonal Antibodies at Age 20: Promise at Last?," <u>Science</u> 270:915-916 (1995)
149.	Hammann et al., "Length Variation of Helix III in a Hammerhead Ribozyme and Its Influence on Cleavage Activity," <u>Antisense & Nucleic Acid Drug Development</u> 9:25-31 (1999)
150.	Hammond et al., "An RNA-Directed Nuclease Mediates Post-Transcriptional Gene Silencing in <i>Drosophila</i> Cells," <u>Nature</u> 404:293-296 (2000)
151.	Hampel and Tritz, "RNA Catalytic Properties of the Minimum (-)sTRSV Sequence," <u>Biochemistry</u> 28:4929-4933 (1989)
152.	Hampel et al., "'Hairpin' Catalytic RNA Model: Evidence for Helices and Sequence Requirement for Substrate RNA," <u>Nucleic Acids Research</u> 18:299-304 (1990)
153.	Harada et al., "Characterization of an established human hepatoma cell line constitutively expressing non-structural proteins of hepatitis C virus by transfection of viral cDNA," <u>Journal of General Virology</u> 76:1215-1221 (1995)
154.	Harris et al., "Identification of phosphates involved in catalysis by the ribozyme RNase P RNA," <u>RNA</u> 1:210-218 (1995)
155.	Haseloff and Gerlach, "Sequences required for self-catalysed cleavage of the satellite RNA of tobacco ringspot virus," <u>Gene</u> 82:43-52 (1989)
156.	Haseloff and Gerlach, "Simple RNA Enzymes with New and Highly Specific Endoribonuclease Activities," <u>Nature</u> 334:585-591 (1988)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

157.	Hayashi et al., "In Vivo Transfection of Rat Liver with Hepatitis C Virus cDNA Using Cationic Liposome-Mediated Gene Delivery," <i>HCD Gene Delivery</i> pp143-149 (1995)
158.	Hegg et al., "Kinetics and Thermodynamics of Intermolecular Catalysis by Hairpin Ribozymes," <i>Biochemistry</i> 34:15813-15828 (1995)
159.	Hermann and Patel, "Adaptive Recognition by Nucleic Acid Aptamers," <i>Science</i> 287:820-825 (2000)
160.	Herschlag and Cech, "Catalysis of RNA Cleavage by the <i>Tetrahymena thermophila</i> Ribozyme 1. Kinetic Description of the Reaction of an RNA Substrate Complementary to the Active Site," <i>Biochemistry</i> 29:10159-10171 (1990)
161.	Herschlag and Cech, "Catalysis of RNA Cleavage by the <i>Tetrahymena thermophila</i> Ribozyme. 2. Kinetic Description of the Reaction of an RNA Substrate That Forms a Mismatch at the Active Site," <i>Biochemistry</i> 29:10172-10180 (1990)
162.	Hertel et al., "A Kinetic Thermodynamic Framework for the Hammerhead Ribozyme Reaction," <i>Biochemistry</i> 33:3374-3385 (1994)
163.	Hertel et al., "Numbering System for the Hammerhead," <i>Nucleic Acids Research</i> 20:3252 (1992)
164.	Hiramatsu et al., "HCV cDNA transfection to HepG2 cells," <i>Journal of Viral Hepatitis</i> 4:61-67 (1997) [sometimes referred to as Haramatsu]
165.	Hofland and Huang, "Formulation and Delivery of Nucleic Acids," <i>Handbook of Exp. Pharmacol.</i> 137:165-192 (1999)
166.	Honda et al., "A Phylogenetically Conserved Stem-Loop Structure at the 5' Border of the Internal Ribosome Entry Site of Hepatitis C Virus is Required for Cap-Independent Viral Translation," <i>Journal of Virology</i> 73:1165-1174
167.	Hoofnagle et al., "The treatment of chronic viral hepatitis," <i>The New England Journal of Medicine</i> 336(5):347-356 (1997)
168.	Horisberger, "MX Protein: Function and Mechanism of Action," <i>Interferon: Principles and Medical Applications</i> pp215-224 (1992)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		Applicant: Beigelman et al.	
		Filing Date:	Group:
		September 23, 2003	1632

169.	Houghton et al., "Molecular Biology of the Hepatitis C Viruses: Implications for Diagnosis, Development and Control of Viral Disease," <u>Hepatology</u> 14(2):381-388 (1991)
170.	Hunziker et al., "Nucleic Acid Analogues: Synthesis and Properties, in Modern Synthetic Methods," <u>VCH</u> , 331-417
171.	Hurwitz et al., "Pharmacodynamics of (-)- β -2',3'-Dideoxy-3'-Thiacytidine in Chronically Virus-Infected Woodchucks Compared to Its Pharmacodynamics in Humans," <u>Antimicrobial Agents and Chemotherapy</u> 42:2804-2809 (1998)
172.	Hutvagner et al., "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the <i>let-7</i> Small Temporal RNA," <u>Science</u> 293:834-838 (2001)
173.	Iacovacci et al., "Molecular Characterization and Dynamics of Hepatitis C Virus Replication in Human Fetal Hepatocytes Infected <i>In Vitro</i> ," <u>Hepatology</u> 26(5):1328-1337 (1997)
174.	Iacovacci et al., "Quantitation of hepatitis C virus RNA production in two human bone marrow-derived B-cell lines infected <i>in vitro</i> ," <u>Institut Pasteur/Elsevier</u> 148:147-151 (1997)
175.	Ilan et al., "The Hepatitis B Virus-Trimera Mouse: A Model for Human HBV Infection and Evaluation of Anti-HBV Therapeutic Agents," <u>Hepatology</u> 553-562 (1999)
176.	Imperial, "New Treatment Strategies in Hepatitis B and C: Natural History of Chronic Hepatitis B and C," <u>Journal of Gastroenterology and Hepatology</u> 14:S1-S5 (1999)
177.	Ishiwata et al., "Physical-Chemistry Characteristics and Biodistribution of Poly(ethylene glycol)-Coated Liposomes Using Poly(oxyethylene) Cholesteryl Ether," <u>Chem. Pharm. Bull.</u> 43:1005-1011 (1995) (mistakenly referred to as Ishiwataet)
178.	Ishizaka et al., "Isolation of Active Ribozymes from an RNA Pool of Random Sequences Using an Anchored Substrate RNA," <u>Biochemical and Biophysical Research Communication</u> 214(2):403-409 (1995)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)			
		Applicant: Beigelman et al.	
		Filing Date: September 23, 2003	Group: 1632

179.	Ito et al., "Cultivation of hepatitis C virus in primary hepatocyte culture from patients with chronic hepatitis C results in release of high titre infectious virus," <u>Journal of General Virology</u> 77:1043-1054 (1996)
180.	Izant and Weintraub, "Constitutive and Conditional Suppression of Exogenous and Endogeneous Genes by Anti-Sense RNA," <u>Science</u> 229:345-352 (1985)
181.	Jaeger et al., "Improved Predictions of Secondary Structures for RNA," <u>Proc. Natl. Acad. Sci. USA</u> 86:7706-7710 (1989)
182.	Jarvis et al., "Optimizing the Cell Efficacy of Synthetic Ribozymes," <u>Journal of Biological Chemistry</u> 271:29107-29112 (1996)
183.	Jayasena, "Aptamers: An Emerging Class of Molecules that Rival Antibodies in Diagnostics," <u>Clinical Chemistry</u> 45:1628-1650 (1999)
184.	Jeffries and Symons, "A Catalytic 13-mer Ribozyme," <u>Nucleic Acids Research</u> 17:1371-1377 (1989) (also referred to as Jefferies)
185.	Johnson et al., "How Interferons Fight Disease," <u>Scientific American</u> , pp. 68-75 (May 1994)
186.	Jolliet-Riant and Tillement, "Drug transfer across the blood-brain barrier and improvement of brain delivery," <u>Fundam. Clin. Pharmacol.</u> 13:16-26 (1999)
187.	Joseph et al., "Substrate selection rules for the hairpin ribozyme determined by in vitro selection, mutation, and analysis of mismatched substrates," <u>Genes & Development</u> 7:130-138 (1993)
188.	Joyce et al., "Amplification, mutation and selection of catalytic RNA," <u>Gene</u> 82:83-87 (1989)
189.	Joyce, "Directed Molecular Evolution," <u>Scientific American</u> 267:90-97 (1992)
190.	Karpeisky et al, "2'-O-Methylthiomethyl Modifications In Hammerhead Ribozymes," <u>Nucleosides & Nucleotides</u> 16(7-9):955-958 (1997) {Mistakenly referred to as Weifeng and Torrence}

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)			
		Applicant: Beigelman et al.	
		Filing Date: September 23, 2003	Group: 1632

191.	Karpeisky et al, "Highly Efficient Synthesis of 2'-O-Amino Nucleosides And Their Incorporation in Hammerhead Ribozymes," <u>Tetrahedron Letters</u> 39:1131-1134 (1998)
192.	Kashani-Sabet et al., "Reversal of the Malignant Phenotype by an Anti-ras Ribozyme," <u>Antisense Research & Development</u> 2:3-15 (1992)
193.	Kato et al., "Molecular structure of the Japanese hepatitis C viral genome," <u>Federation of European Biochemical Societies</u> 280(2):325-328 (1991)
194.	Kato et al., "Susceptibility of Human T-Lymphotropic Virus Type I Infected Cell Line MT-2 Hepatitis C Virus Infection ¹ ," <u>Biochemical and Biophysical Research Communications</u> 206(3):863-869 (1995)
195.	Kawamura et al., "Transgenic Expression of Hepatitis C Virus Structural Proteins in the Mouse," <u>Hepatology</u> 25(4):1014-1021 (1997)
196.	Kidd et al., "A Revised Secondary Structure Model for the 3'-end of Hepatitis B Virus Pregenomic RNA," <u>Nucleic Acids Research</u> 24:3295-3301 (1996)
197.	Kim and Cech, "Three-dimensional model of the active site of the self-splicing rRNA precursor of <i>Tetrahymena</i> ," <u>Proc. Natl. Acad. Sci. USA</u> 84:8788-8792 (1987)
198.	Kim et al., "Repression of Hepatitis B Virus X Gene Expression by Hammerhead Ribozymes," <u>Biochemical and Biophysical Research Comm.</u> 257:759-765 (1999)
199.	Knitt et al., "ph Dependencies of the <i>Tetrahymena</i> Ribozyme Reveal an Unconventional Origin of an Apparent pK _a ," <u>Biochemistry</u> 35:1560-1570 (1996)
200.	Koike et al., "Expression of hepatitis C virus envelope proteins in transgenic mice," <u>Journal of General Virology</u> 76:3031-3038 (1995)
201.	Kollmann et al., "The Concurrent Maturation of Mouse and Human Thymocytes in Human Fetal Thymus Implanted in NIH-beige-nude-xid Mice Is Associated with the Reconstitution of the Murine Immune System," <u>J. Exp. Med.</u> 177:821-832 (1993)
202.	Kore, et al., "Sequence specificity of the hammerhead ribozyme revisited; the NIH rule," <u>Nucleic Acids Research</u> , 26(18):4116-4120 (1998).

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

203.	Kumar and Ellington, "Artificial evolution and natural ribozymes," <u>FASEB J.</u> 9:1183-1195 (1995)
204.	Kusser, "Chemically modified nucleic acid aptamers for in vitro selections: evolving evolution," <u>Reviews in Molecular Biotechnology</u> 74:27-38 (2000)
205.	Lasic and Needham "The 'Stealth' Liposome: A Prototypical Biomaterial," <u>Chemical Reviews</u> 95:2601-2627 (1995)
206.	Lasic and Papahadjopoulos, "Liposomes Revisited," <u>Science</u> 267:1275-1276 (1995)
207.	Lee and Larson, "Modified Liposome Formulations for Cytosolic Delivery of Macromolecules," <u>ACS Symposium Series</u> 752:184-192 (2000)
208.	Lee and Lee, "Preparation of Cluster Glycosides of N-Acetylgalactosamine That Have Subnanomolar Binding Constants Towards the Mammalian Hepatic Gal/GalNAc-specific Receptor," <u>Glyconjugates J.</u> 4:317-328 (1987)
209.	Lee et al., "Stimulation of Natural Killer Cell Activity and Inhibition of Proliferation of Various Leukemic Cells by Purified Human Leukocyte Interferon Subtypes," <u>Cancer Research</u> 42:1312-1316 (1982)
210.	Leinbach et al., "Substrate Specificity of the NS3 Serine Proteinase of Hepatitis C Virus as Determined by Mutagenesis at the NS3/NS4A Junction," <u>Virology</u> 204:163-169 (1994)
211.	Leventhal et al., "Long-Term Response of Recurrent Respiratory Papillomatosis to Treatment with Lymphoblastoid Interferon Alfa-n1," <u>The New England Journal of Medicine</u> 325(9):613-617 (1991)
212.	L'Huillier et al., "Cytoplasmic Delivery of Ribozymes Leads to Efficient Reduction in α -Lactalbumin mRNA Levels in C1271 Mouse," <u>EMBO J.</u> 11:4411-4418 (1992)
213.	Li and Altman, "Cleavage by RNase P of gene N mRNA reduces bacteriophage λ burst size," <u>Nucleic Acids Research</u> 24:835-842 (1996)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

214.	Li et al., "Thermodynamic and Activation Parameters for Binding of a Pyrene-Labeled Substrate by the <i>Tetrahymena</i> Ribozyme: Docking is Not Diffusion-Controlled and is Driven by a Favorable Entropy Change," <u>Biochemistry</u> 34:14394-14399 (1995)
215.	Liang et al., "Viral Pathogenesis of Hepatocellular Carcinoma in the United States," <u>Hepatology</u> 18(6):1326-1333 (1993)
216.	Lieber et al., "Stable High-Level Gene Expression in Mammalian Cells by T7 Phage RNA Polymerase," <u>Methods Enzymol.</u> 217:47-66 (1993)
217.	Lieber et al., "Elimination of Hepatitis C Virus RNA in Infected Human Hepatocytes by Adenovirus-Mediated Expression of Ribozymes," <u>Journal of Virology</u> 70:8782-8791 (1996)
218.	Limbach et al., "Summary: the modified nucleosides of RNA," <u>Nucleic Acids Research</u> 22(12):2183-2196 (1994)
219.	Lin and Matteucci, "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acid," <u>J. Am. Chem. Soc.</u> 120:8531-8532 (1998)
220.	Lisacek et al., "Automatic Identification of Group I Intron Cores in Genomic DNA Sequences," <u>J. Mol. Biol.</u> 235:1206-1217 (1994)
221.	Liszewicz et al., "Inhibition of Human Immunodeficiency Virus Type 1 Replication by Regulated Expression of a Polymeric Tat Activation Response RNA Decoy as a Strategy for Gene Therapy in AIDS," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 90:8000-8004 (1993)
222.	Liu et al., "Cationic Liposome-mediated Intravenous Gene Delivery," <u>J. Biol. Chem.</u> 270(42):24864-24870 (1995)
223.	Lixia et al., "Blocking Effect of Hammerhead Ribozyme RCP on HBV Gene Expression in HepG2215 Cell Line," <u>J. Med. Coll. PLA</u> 13:157-159 (1998) [mistakenly referred to as Gan]
224.	Lixia et al., "Effects of Hammerhead Ribozyme (RCP) on HBV P Gene <i>In Vitro</i> ," <u>J. Med. Coll. PLA</u> 11:171-175 (1996) [mistakenly referred to as Gan]

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

225.	Long and Uhlenbeck, "Kinetic characterization of intramolecular and intermolecular hammerhead RNAs with stem II deletions," <u>Proc. Natl. Acad. Sci. USA</u> 91:6977-6981 (1994)
226.	Lu et al., "Poliovirus chimeras replicating under the translational control of genetic elements of hepatitis C virus reveal unusual properties of the internal ribosomal entry site of hepatitis C virus," <u>Proc. Natl. Acad. Sci. USA</u> 93:1412-1417 (1996)
227.	Macejak et al., "Inhibition of Hepatitis C Virus (HCV)-RNA-Dependent Translation and Replication of a Chimeric HCV Poliovirus Using Synthetic Stabilized Ribozymes," <u>Hepatology</u> 31(3):769-776 (2000)
228.	Maher et al., "Kinetic Analysis of Oligodeoxyribonucleotide-Directed Triple-Helix Formation on DNA," <u>Biochemistry</u> 29:8820-8826 (1990)
229.	Marcellin et al., "Recombinant Human α -Interferon in Patients with Chronic Non-A, Non-B Hepatitis: A Multicenter Randomized Controlled Trial from France," <u>Hepatology</u> 13(3):393-397 (1991)
230.	Marcellin et al., "Recombinant Human α -Interferon in Patients with Chronic Non-A, Non-B Hepatitis: A Multicenter Randomized Controlled Trial from France," <u>Hepatology</u> 13(3):393-397 (1991)
231.	Maurer et al., "Lipid-based systems for the intracellular delivery of genetic drugs," <u>Molecular Membrane Biology</u> 16:129-140 (1999)
232.	McGarry and Lindquist, "Inhibition of heat shock protein synthesis by heat-inducible antisense RNA," <u>Proc. Natl. Acad. Sci. USA</u> 83:399-403 (1986)
233.	McKay, "Structure and function of the hammerhead ribozyme: an unfinished story," <u>RNA</u> 2:395-403 (1996)
234.	Mesmaeker et al, "Novel Backbone Replacements for Oligonucleotides," <u>American Chemical Society</u> , pp. 24-39 (1994)
235.	Michel and Westhof, "Slippery substrates," <u>Nat. Struct. Biol.</u> 1:5-7 (1994)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 02-249-E (400.042)	Serial No. 10/669,841
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		Applicant: Beigelman et al.	
		Filing Date: September 23, 2003	Group: 1632

236.	Michel et al., "Structure and Activities of Group II Introns," <u>Annu. Rev. Biochem.</u> 64:435-461 (1995)
237.	Michels and Pyle, "Conversion of a Group II Intron into a New Multiple-Turnover Ribozyme that Selectively Cleaves Oligonucleotides: Elucidation of Reaction Mechanism and Structure/Function Relationships," <u>Biochemistry</u> 34:2965-2977 (1995)
238.	Milligan and Uhlenbeck, "Synthesis of Small RNAs Using T7 RNA Polymerase," <u>Methods Enzymol.</u> 180:51-62 (1989)
239.	Milner et al., "Selecting effective antisense reagents on combinatorial oligonucleotide arrays," <u>Nature Biotechnology</u> 15:537-541 (1997)
240.	Mitra et al., "A mammalian 2-5A system functions as an antiviral pathway in transgenic plants," <u>Proc. Natl. Acad. Sci. USA</u> 93:6780-6785 (1996)
241.	Mizuno et al., "Virion-like Structures in HeLa G Cells Transfected with the Full-Length Sequence of the Hepatitis C Virus Genome," <u>Gastroenterology</u> 109:1933-1940 (1995)
242.	Mizutani et al., "Characterization of Hepatitis C Virus Replication in Cloned Cells Obtained from a Human T-Cell Leukemia Virus Type 1-Infected Cell Line, MT-2," <u>Journal of Virology</u> 70(10):7219-7223 (1996)
243.	Mizutani et al., "Long-Term Human T-Cell Culture System Supporting Hepatitis C Virus Replication," <u>Biochemical and Biophysical Research Communications</u> 227:822-826 (1996)
244.	Moore and Sharp, "Site-Specific Modification of Pre-mRNA: The 2'-Hydroxyl Groups at the Splice Sites," <u>Science</u> 256:992-996 (1992)
245.	Moriya et al., "Hepatitis C virus core protein induces hepatic steatosis in transgenic mice," <u>Journal of General Virology</u> 78:1527-1531 (1997)
246.	Morrey et al., "Utilization of Transgenic Mice Replicating High Levels of Hepatitis B Virus for Antiviral Evaluation of Lamivudine," <u>Antiviral Research</u> 42:97-108 (1999)
247.	Mukhopadhyay et al., "Antisense Regulation of Oncogenes in Human Cancer," <u>Critical Reviews in Oncogenesis</u> 7:151-190 (1996)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		02-249-E (400.042)	10/669,841
		Applicant: Beigelman et al.	
		Filing Date:	Group:
		September 23, 2003	1632

248.	Nakajima et al., "Characterization of Long-Term Cultures of Hepatitis C Virus," <u>Journal of Virology</u> 70(5):3325-3329 (1996)
249.	Nakamaye and Eckstein, "AUA-Cleaving Hammerhead Ribozymes: Attempted Selection for Improved Cleavage," <u>Biochemistry</u> 33:1271-1277 (1994)
250.	Nathans and Smith, "Restriction Endonucleases in the Analysis and Restructuring of DNA Molecules," <u>Ann. Rev. Biochem.</u> 44:273-293 (1975)
251.	Noonberg et al., <i>In vivo</i> generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation," <u>Nucleic Acids Research</u> 22(14):2830-2836 (1994)
252.	Nykanen et al., "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," <u>Cell</u> 107:309-321 (2001)
253.	Ohkawa et al., "Activities of HIV-RNA Targeted Ribozymes Transcribed From a 'Shot-Gun' Type Ribozyme-trimming Plasmid," <u>Nucleic Acids Symp. Ser.</u> 27:15-16 (1992)
254.	Ohkawa et al., "Cleavage of viral RNA and inhibition of viral translation by hepatitis C virus RNA-specific hammerhead ribozyme <i>in vitro</i> ," <u>Journal of Hepatology</u> 27:78-84 (1997)
255.	Ojwang et al., "Inhibition of Human Immunodeficiency Virus Type 1 Expression by a Hairpin Ribozyme," <u>Proc. Natl. Acad. Sci. USA</u> 89:10802-10806 (1992)
256.	Okamoto et al., "Nucleotide sequence of the genomic RNA of hepatitis C virus isolated from a human carrier: comparison with reported isolates for conserved and divergent regions," <u>Journal of General Virology</u> 72:2697-2704 (1991)
257.	Oku et al., "Real-time analysis of liposomal trafficking in tumor-bearing mice by use of positron emission tomography," <u>Biochimica et Biophysica Acta</u> 1238:86-90 (1995)
258.	Orgel, "Selection <i>in vitro</i> ," <u>Proc. R. Soc. London B.</u> 205:435-442 (1979)
259.	Ozes et al., "A Comparison of Interferon-Con1 with Natural Recombinant Interferons- α : Antiviral, Antiproliferative, and Natural Killer-Inducing Activities," <u>Journal of Interferon Research</u> 12:55-59 (1992)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

260.	Pace and Smith, "Ribonuclease P: Function and Variation," <i>J. Biol. Chem.</i> 265:3587-3590 (1990)
261.	Pan et al., "Probing of tertiary interactions in RNA: 2'-Hydroxyl-base contacts between the Rnase P and pre-tRNA," <i>Proc. Natl. Acad. Sci. USA</i> 92:12510-12514 (1995)
262.	Pardridge et al., "Vector-mediated delivery of a polyamide ("peptide") nucleic acid analogue through the blood-brain barrier <i>in vivo</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 92:5592-5596 (1995)
263.	Pasquinelli et al., "Hepatitis C Virus Core and E2 Protein Expression in Transgenic Mice," <i>Hepatology</i> 25(3):719-727 (1997)
264.	Passman et al., " <i>In Situ</i> Demonstration of Inhibitory Effects of Hammerhead Ribozymes that are Targeted to the Hepatitis Bx Sequence in Cultured Cells," <i>Biochemical and Biophysical Research Communications</i> 268:728-733 (2000)
265.	Perreault et al., "Mixed Deoxyribo- and Ribo-Oligonucleotides with Catalytic Activity," <i>Nature</i> 344:565-567 (1990) (often mistakenly listed as Perrault)
266.	Perrotta and Been, "A pseudoknot-like structure required for efficeint self-cleavage of hepatitis delta virus RNA," <i>Nature</i> 350:434-436 (1991)
267.	Perrotta and Been, "Cleavage of Oligoribonucleotides by a Ribozyme Derived from the Hepatitis δ Virus RNA Sequence," <i>Biochemistry</i> 31:16-21 (1992)
268.	Pestka et al., "Interferons and Their Actions," <i>Ann. Rev. Biochem.</i> 56:727-777 (1987)
269.	Pestka, "[1] Interferon from 1981 to 1986," <i>Methods in Enzymology</i> 119:3-15 (1986)
270.	Pfeffer and Strulovici, "Transmembrane Secondary Messengers for IFN α/β <i>Interferon. Principles and Medical Applications</i> 151-160 (1992)
271.	Pichlmayr et al., "Indications for Liver Transplantation in Heptobiliary Malignancy," <i>Hepatology</i> 20:33S-40S (1994)
272.	Pieken et al., "Kinetic Characterization of Ribonuclease-Resistant 2'-Modified Hammerhead Ribozymes," <i>Science</i> 253:314-317 (1991)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

273.	Player and Torrence, "The 2-5A System: Modulation of Viral and Cellular Processes Through Acceleration of RNA Degradation," <i>Pharmacol Ther.</i> 78:55-113 (1998)
274.	Ponpipom et al., "Cell-Specific Ligands for Selective Drug Delivery to Tissues and Organs," <i>J. Med. Chem.</i> 24:1388-1395 (1981)
275.	Putlitz et al., "Combinatorial Screening and Intracellular Antiviral Activity of Hairpin Ribozymes Directed Against Hepatitis B Virus," <i>Journal of Virology</i> 73:5381-5387 (1999)
276.	Puttaraju et al., "A circular trans-acting hepatitis delta virus ribozyme," <i>Nucleic Acids Research</i> 21:4253-4258 (1993)
277.	Pyle et al., "Building a Kinetic Framework for Group II Intron Ribozyme Activity: Quantitation of Interdomain Binding and Reaction Rate," <i>Biochemistry</i> 33:2716-2725 (1994)
278.	Pyle et al., "Building a Kinetic Framework for Group II Intron Ribozyme Activity: Quantitation of Interdomain Binding and Reaction Rate," <i>Biochemistry</i> 33:2716-2725 (1994)
279.	Robertson et al., "Purification and Properties of a Specific <i>Escherichia coli</i> Ribonuclease which Cleaves a Tyrosine Transfer Ribonucleic Acid Precursor," <i>J. Biol. Chem.</i> 247:5243-5251 (1972)
280.	Rossi et al., "Ribozymes as Anti-HIV-1 Therapeutic Agents: Principles, Applications, and Problems," <i>Aids Research and Human Retroviruses</i> 8:183-189 (1992)
281.	Rubinstein, "Multiple Interferon Subtypes: The Phenomenon and Its Relevance," <i>Journal of Interferon Research</i> 7:545-551 (1987)
282.	Ruiz et al., "Design and Preparation of a Multimeric Self-Cleaving Hammerhead Ribozyme," <i>BioTechniques</i> 22:338-345 (1997)
283.	Sakamoto et al., "Intracellular Cleavage of Hepatitis C Virus RNA and Inhibition of Viral Protein Translation by Hammerhead Ribozymes," <i>J. Clin. Invest., The American Society for Clinical Investigation, Inc.</i> 98(12):2720-2728 (1996)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

284.	Samuel, "The RNA-Dependent PI/eIF-2 α Protein Kinase," <i>Interferon: Principles & Medical Applications</i> pp237-249 (1992)
285.	Santoro and Joyce, "A general purpose RNA-cleaving DNA enzyme," <i>Proc. Natl. Acad. Sci. USA</i> 94:4262-4266 (1997)
286.	Santoro et al., "Mechanism and Utility of an RNA-Cleaving DNA Enzyme," <i>Biochemistry</i> 37:13330-13342 (1998)
287.	Santoro et al., "RNA Cleavage by a DNA Enzyme with Extended Chemical Functionality," <i>J. Am. Chem. Soc.</i> 122:2433-2439 (2000)
288.	Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents" <i>Science</i> 247:1222-1225 (1990)
289.	Saville and Collins, "A Site-Specific Self-Cleavage Reaction Performed by a Novel RNA In <i>Neurospora</i> Mitochondria," <i>Cell</i> 61:685-696 (1990)
290.	Saville and Collins, "RNA-Mediated Ligation of Self-Cleavage Products of a <i>Neurospora</i> Mitochondrial Plasmid Transcript," <i>Proc. Natl. Acad. Sci. USA</i> 88:8826-8830 (1991)
291.	Scanlon et al., "Ribozyme-Mediated Cleavage of c-fos mRNA Reduces Gene Expression of DNA Synthesis Enzymes and Metallothionein," <i>Proc. Natl. Acad. Sci. USA</i> 88:10591-10595 (1991)
292.	Scaringe et al., "Chemical synthesis of biologically active oligoribonucleotides using β -cyanoethyl protected ribonucleoside phosphoramidites," <i>Nucl Acids Res.</i> 18:5433-5441 (1990)
293.	Schmajuk et al., "Antisense Oligonucleotides with Different Backbones," <i>The Journal of Biological Chemistry</i> 274:21783-21789 (1999)
294.	Schmidt et al., "Base and sugar requirements for RNA cleavage of essential nucleoside residues in internal loop B of the hairpin ribozyme: implications for secondary structure," <i>Nucleic Acids Research</i> 24:573-581 (1996)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

295.	Schroeder et al., "Diffusion Enhancement of Drugs by Loaded Nanoparticles in Vitro," <i>Prog. Neuro-Psychopharmacol. & Biol. Psychiat.</i> 23:941-949 (1999) [sometimes cited by RPI as <i>Prog Neuropsychopharmacol Biol Psychiatry</i> 23:941-949, 1999]
296.	Scott et al., "The crystal structure of an All-RNA hammerhead ribozyme: A proposed mechanism for RNA catalytic cleavage," <i>Cell</i> 81:991-1002 (1995)
297.	Seipp et al., "Establishment of persistent hepatitis C virus infection and replication <i>in vitro</i> ," <i>Journal of General Virology</i> 78:2467-2476 (1997)
298.	Sells et al., "Production of Hepatitis B Virus Particles in Hep G2 Cells Transfected with Cloned Hepatitis B Virus DNA," <i>Proc. Natl. Acad. Sci.</i> 84:1005-1009 (1987)
299.	Shabarova et al., "Chemical ligation of DNA: The first non-enzymatic assembly of a biologically active gene," <i>Nucleic Acids Research</i> 19:4247-4251 (1991)
300.	Sherlock, "Viral hepatitis," <i>The Lancet</i> 339:802 (1992)
301.	Silverman et al., "Selective RNA Cleavage by Isolated RNase L Activated with 2-5A Antisense Chimeric Oligonucleotides," <i>Methods in Enzymology</i> 313:522-533 (1999)
302.	Simmonds et al., "Identification of genotypes of hepatitis C virus by sequence comparisons in the core, E1 and NS-5 regions," <i>Journal of General Virology</i> 75:1053-1061 (1994)
303.	Simmonds, "Variability of Hepatitis C Virus," <i>Hepatology</i> 21:570-583 (1995)
304.	Smith and Simmonds, "Characteristics of Nucleotide Substitution in the Hepatitis C Virus Genome: Constraints on Sequence Change in Coding Regions at Both Ends of the Genome," <i>J. Mol. Evol.</i> 45:238-246 (1997)
305.	Stein and Cheng, "Antisense Oligonucleotides as Therapeutic Agents - Is the Bullet Really Magical?" <i>Science</i> 261:1004-1288 (1993)
306.	Stein et al., "A Specificity Comparison of Four Antisense Types: Morpholino, 2'-O-Methyl RNA, DNA, and Phosphorothioate DNA," <i>Antisense & Nucleic Acid Drug Development</i> 7:151-157 (1997)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

307.	Strobel and Dervan, "Site-Specific Cleavage of a Yeast Chromosome by Oligonucleotide-Directed Triple-Helix Formation," <i>Science</i> 249:73-75 (1990)
308.	Strobel et al., "Exocyclic Amine of the Conserved G-U Pair at the Cleavage Site of the <i>Tetrahymena</i> Ribozyme Contributes to 5'-Splice Site Selection and Transition State Stabilization," <i>Biochemistry</i> 35:1201-1211 (1996)
309.	Strobel et al., "Minor Groove Recognition of the Conserved G-U Pair at the <i>Tetrahymena</i> Ribozyme Reaction Site," <i>Science</i> 267:675-679 (1995)
310.	Sullenger and Cech, "Ribozyme-mediated repair of defective mRNA by targeted trans-splicing," <i>Nature</i> 371:619-622 (1994)
311.	Sullenger and Cech, "Tethering Ribozymes to a Retroviral Packaging Signal for Destruction of Viral RNA," <i>Science</i> 262:1566-1569 (1993)
312.	Sullenger et al., "Overexpression of TAR Sequences Renders Cells Resistant to Human Immunodeficiency Virus Replication," <i>Cell</i> 63:601-608 (1990)
313.	Sun, "Technology evaluation: SELEX, Giliad Sciences Inc," <i>Current Opinion in Molecular Therapeutics</i> 2:100-105 (2000)
314.	Symons, "Ribozymes," <i>Current Opinion in Structural Biology</i> 4(3):322-330 (1994)
315.	Szostak, " <i>In Vitro</i> Genes," <i>TIBS</i> 17:89-93 (1993)
316.	Tagawa et al., "Infection of human hepatocyte cell lines with hepatitis C virus <i>in vitro</i> ," <i>Journal of Gastroenterology and Hepatology</i> 10:523-527 (1995)
317.	Taira et al., "Construction of a novel RNA-transcript-trimming plasmid which can be used both <i>in vitro</i> in place of run-off and (G)-free transcriptions and <i>in vivo</i> as multi-sequences transcription vectors," <i>Nucleic Acids Research</i> 19:5125-5130 (1991)
318.	Takahashi et al., "Natural Course of Chronic Hepatitis C," <i>The American Journal of Gastroenterology</i> 88(2):240-243 (1993)
319.	Takehara et al., "Expression of the Hepatitis C Virus Genome in Rat Liver After Cationic Liposome-Mediated <i>In Vivo</i> Gene Transfer," <i>Hepatology</i> 21:746-751 (1995)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

320.	Tang et al., "Examination of the catalytic fitness of the hammerhead ribozyme by in vitro selection," <u>RNA</u> 3:914-925 (1997)
321.	Thompson et al., "Improved accumulation and activity of ribozymes expressed from a tRNA-based RNA polymerase III promoter," <u>Nucleic Acids Research</u> 23:2259-2268 (1995)
322.	Tong et al., "Evidence for Hepatitis C Viral Infection in Patients With Primary Hepatocellular Carcinoma," <u>West J Med</u> 160:133-138 (1994)
323.	Tong et al., "Prediction of Response During Interferon Alfa 2b Therapy in Chronic Hepatitis C Patients Using Viral and Biochemical Characteristics: A Comparison," <u>Hepatology</u> 26(6):1640-1645 (1997)
324.	Tong et al., "Treatment of Chronic Hepatitis C With Consensus Interferon: A Multicenter, Randomized, Controlled Trial," <u>Hepatology</u> 26(3):747-754 (1997)
325.	Torrence et al., "Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense chimera," <u>Proc. Natl. Acad. Sci. USA</u> 90:1300-1304 (1993)
326.	Trinchet et al., "Carcinome Hépatocellulaire: Traitement par Chimioembolisation Artérielle," <u>Presse Med</u> 23(18):831-3 (1994)
327.	Turner et al., "Improved Parameters for Prediction of RNA Structure," <u>Cold Spring Harbor Symposia on Quantitative Biology</u> Volume LII, pp. 123-133 (1987)
328.	Turner et al., "Free Energy Increments for Hydrogen Bonds in Nucleic Acid Base Pairs," <u>J. Am. Chem. Soc.</u> 109:3783-3785 (1987)
329.	Tyler et al., "Peptide nucleic acids targeted to the neurotensin receptor and administered i.p. cross the blood-brain barrier and specifically reduce gene expression," <u>Proc. Natl. Acad. Sci. USA</u> 96:7053-7058 (1999)
330.	Tyler et al., "Specific gene blockade shows that peptide nucleic acids readily enter neuronal cells in vivo," <u>FEBS Letters</u> 421:280-284 (1998)
331.	Uhlenbeck, "A Small Catalytic Oligoribonucleotide," <u>Nature</u> 328:596-600 (1987)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No.	Serial No.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	02-249-E (400.042)	10/669,841	Applicant: Beigelman et al.
	Filing Date:	Group:	September 23, 2003
			1632

332.	Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle," <u>Chemical Reviews</u> 90:544-584 (1990)
333.	Usman and Cedergren, "Exploiting the chemical synthesis of RNA," <u>TIBS</u> 17:334-339 (1992)
334.	Usman and McSwiggen, "Ch. 30 - Catalytic RNA (Ribozymes) as Drugs," <u>Annual Reports in Medicinal Chemistry</u> 30:285-294 (1995)
335.	Usman et al., "Automated Chemical Synthesis of Long Oligoribonucleotides Using 2'-O-Silylated Ribonucleoside 3'-O-Phosphoramidites on a Controlled-Pore Glass Support: Synthesis of a 43-Nucleotide Sequence Similar to the 3'-Half Molecule of an <i>Escherichia coli</i> Formylmethoionine tRNA," <u>J. Am. Chem. Soc.</u> 109:7845-7854 (1987)
336.	Usman et al., "Chemical modification of hammerhead ribozymes: activity and nuclease resistance," <u>Nucleic Acids Symposium Series</u> 31:163-164 (1994)
337.	Usman et al., "Hammerhead ribozyme engineering," <u>Current Opinion in Structural Biology</u> 1:527-533(1996)
338.	Vaish et al., "Isolation of Hammerhead Ribozymes with Altered Core Sequences by <i>in Vitro</i> Selection," <u>Biochemistry</u> 36:6495-6501 (1997)
339.	Valli et al., "Detection of a 5' UTR variation in the HCV genome after long-term <i>in vitro</i> infection," <u>Institut Pasteur/Elsevier</u> 146:285-288 (1995)
340.	Ventura et al., "Activation of HIV-Specific Ribozyme Activity by Self-Cleavage," <u>Nucleic Acids Research</u> 21:3249-3255 (1993)
341.	Verma and Eckstein, "Modified Oligonucleotides: Synthesis and Strategy for Users," <u>Annu. Rev. Biochem.</u> 67:99-134 (1998)
342.	Wands et al., "Nucleic Acid-based Antiviral and Gene Therapy of Chronic Hepatitis B Infection," <u>Jour. of Gastroenterology and Hepatology</u> 12:S354-S369 (1997)
343.	Wang et al., "Translation of Human Hepatitis C Virus RNA in Cultured Cells Is Mediated by an Internal Ribosome-Binding Mechanism," <u>Journal of Virology</u> 67(6):3338-3344 (1993)

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

344.	Warashina, et al., "Extremely High and Specific Activity of DNA Enzymes in Cells with a Philadelphia Chromosome, <u>Chemistry & Biology</u> , 6(4):237-250 (1999)
345.	Weerasinghe et al., "Resistance to Human Immunodeficiency Virus Type 1 (HIV-1) Infection in Human CD4 ⁺ Lymphocyte-Derived Cell Lines Conferred by Using Retroviral Vectors Expressing an HIV-1 RNA-Specific Ribozyme," <u>Journal of Virology</u> 65:5531-5534 (1994)
346.	Welch et al., "A potential therapeutic application of hairpin ribozymes: <i>in vitro</i> and <i>in vivo</i> studies of gene therapy for hepatitis C virus infection," <u>Gene Therapy</u> 3:994-1001 (1996)
347.	Welch et al., "Intracellular Application of Hairpin Ribozyme Genes Against Hepatitis B Virus," <u>Gene Therapy</u> 4:736-743 (1997)
348.	Werner and Uhlenbeck, "The effect of base mismatches in the substrate recognition helices of hammerhead ribozymes on binding and catalysis," <u>Nucleic Acids Research</u> 23:2092-2096 (1995)
349.	Wianny and Zernicka-Goetz et al., "Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development," <u>Nature Cell Biology</u> 2:70-75 (2000)
350.	Wincott et al., "Synthesis, deprotection, analysis and purification of RNA and ribozymes," <u>Nucleic Acids Research</u> 23(14):2677-2684 (1995)
351.	Wincott et al., "A Practical Method for the Production of RNA and Ribozymes," <u>Methods in Molecular Biology</u> 74:59-69 (1997)
352.	Woolf et al., "Specificity of Antisense Oligonucleotides <i>in vivo</i> ," <u>Proc. Natl. Acad. Sci. USA</u> 89:7305-7309 (1992)
353.	Wu and Wu, "Receptor-mediated <i>in Vitro</i> Gene Transformation by a Soluble DNA Carrier System," <u>The Journ. of Biol. Chem.</u> 262:4429-4432 (1987)
354.	Wu-Pong, "Oligonucleotides: Opportunities for Drug Therapy and Research," <u>BioPharm</u> pp20-33 (1994)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449 (Rev. 2-32)	U.S. Department of Commerce Patent and Trademark Office	Att. Docket No.	Serial No.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)		02-249-E (400.042)	10/669,841
		Applicant: Beigelman et al.	
		Filing Date:	Group:
		September 23, 2003	1632

355.	Yamamoto et al., " <i>In Vivo</i> Transfection of Hepatitis C Virus Complementary DNA Into Rodent Liver by Asialoglycoprotein Receptor Mediated Gene Delivery," <u>Hepatology</u> 22(3):847-855 (1995)
356.	Yoo et al., "Transfection of a Differentiated Human Hepatoma Cell Line (Huh7) with In Vitro-Transcribed Hepatitis C Virus (HCV) RNA and Establishment of a Long-Term Culture Persistently Infected with HCV," <u>Journal of Virology</u> 69(1):32-38 (1995)
357.	Yu et al., "A Hairpin Ribozyme Inhibits Expression of Diverse Strains of Human Immunodeficiency Virus Type 1," <u>Proc. Natl. Acad. Sci. USA</u> 90:6340-6344 (1993)
358.	Yuan et al., "Targeted cleavage of mRNA by human RNase P," <u>Proc. Natl. Acad. Sci. USA</u> 89:8006-8010 (1992)
359.	Zarrinkar and Williamson, "The P9.1-P9.2 peripheral extension helps guide folding of the <i>Tetrahymena</i> ribozyme," <u>Nucleic Acids Research</u> 24:854-858 (1996)
360.	Zaug et al., "The <i>Tetrahymena</i> Ribozyme Acts Like an RNA Restriction Endonuclease," <u>Nature</u> 324:429-433 (1986)
361.	Zhiqiang et al., " <i>In Vivo</i> Inhibition of Hepatitis B Viral Gene Expression by Antisense Phosphorothioate Oligodeoxynucleotides in Athymic Nude Mice," <u>Journal of Viral Hepatitis</u> 3:19-22 (1996) [mistakenly referred to as Yao]
362.	Zhou et al., "Synthesis of Functional mRNA in Mammalian Cells by Bacteriophage T3 RNA Polymerase," <u>Mol. Cell. Biol.</u> 10:4529-4537 (1990)
363.	Zimmerly et al., "A Group II Intron RNA is a Catalytic Component of a DNA Endonuclease Involved in Intron Mobility," <u>Cell</u> 83:529-538 (1995)
364.	Bahramian et al., "Transcriptional and Posttranscriptional Silencing of Rodent $\alpha 1(I)$ Collagen by a Homologous Transcriptionally Self-Silenced Transgene," <u>Molecular and Cellular Biology</u> , 19:274-283 (1999)
365.	Hamilton, et al., "A Species of Small Antisense RNA in Posttranscriptional Gene Silencing in Plants," <u>Science</u> , 286, 950-952 (1999)
366.	International Search Report for PCT/US03/05043 mailed January 16, 2004

EXAMINER	DATE CONSIDERED
----------	-----------------

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

FORM PTO-1449
(Rev. 2-32)

U.S. Department of Commerce
Patent and Trademark Office

Atty. Docket No.

02-249-E
(400.042)

Serial No.

10/669,841

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use several sheets if necessary)

Applicant:

Beigelman et al.

Filing Date:

September 23, 2003

Group:

1632

367.	McCaffrey et al., "RNA interference in adult mice," <i>Nature</i> , 418, 38-39 (2002)
368.	Randall et al., "Clearance of replicating hepatitis C virus replicon RNAs in cell culture by small interfering RNAs," <i>PNAS</i> , 100:1, 235-240 (2003)
369.	Lin et al., "Policing rogue genes," <i>Nature</i> , 402, 128-129 (1999)
370.	Sharp et al., "RNAi and double-strand RNA," <i>Genes & Development</i> , 13:139-141 (1999)
371.	Strauss, Evelyn, "Molecular Biology: Candidate 'Gene Silencers' Found," <i>Molecular Biology</i> , Vol. 286, No. 5441, p. 886 (1999) [sometimes mistakenly referred to as being published in <i>Science</i>]
372.	Tuschl et al., "Targeted mRNA Degradation by Double-Stranded RNA In Vitro," <i>Genes & Development</i> 13:3191-3197 (1999)
373.	Waterhouse et al., "Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA," <i>Proc. Natl. Acad. Sci. USA</i> , 95, 13959-13964 (1998)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.